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CHAPTER CLXXXVIII

DISEASES OF THE SKIN

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The cutaneous disorders described in this section are divided into seven classes, discussed as follows:

I. AFFECTIONS OF CONGENITAL ORIGIN

BY CLARK WYLIE FINNERUD, M.D., AND ERWIN PAUL ZEISLER, M.D.
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II. INFECTIOUS DISEASES OF THE SKIN

BY OLIVER S. ORMSBY, M.D.
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III. ARTIFICIAL DERMATOSES (KNOWN ETIOLOGY)

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IV. DERMATOSES OF UNKNOWN ETIOLOGY

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V. HYPERTROPHIES, ATROPHIES, NEUROSES AND ANOMALIES OF PIGMENTATION

BY JAMES HERBERT MITCHELL, M.D.
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VI. NEW GROWTHS (ACQUIRED)

BY ERWIN PAUL ZEISLER, M.D.
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VII. DISEASES OF THE APPENDAGES OF THE SKIN

BY ARTHUR W. STILLIANS, M.D.
CHICAGO, ILL.

CLASS I: Affections of Congenital Origin.
  A. Superficial Congenital Affections
    Ichthyosis
      Ichthyosis congenita
      Ichthyosis hystrix
      Erythrodermie congenitale ichthyosiforme
    Keratolysis
    Keratodermia palmaris et plantaris
    Millium congenitale (en plaques)
    Congenital hirsuties
    Alopecia congenita
    Albinism

- Xeroderma pigmentosum
- Epidermolysis bullosa hereditaria
- Sclerema neonatorum
- Edema neonatorum.

B. Congenital New Growths of the Skin
- Nevus vasculosus
- Nevus pigmentosus
- Lymphangioma circumscriptum
- Adenoma sebaceum
- Multiple benign cystic epithelioma
- Neurofibroma—(von Recklinghausen's disease)
- Xanthoma
- Dermoid cysts
- Leiomyoma cutis.

CLASS II: Infectious Diseases of the Skin.

A. Diseases Caused by Cocci
- Impetigo
  - Pemphigus neonatorum
  - Ecthyma
- Dermatitis vegetans in infants
- Dermatitis exfoliativa neonatorum
- Dermatitis gangrenosa infantum
- Erysipelas
- Erysipeloid
- Multiple abscesses of the skin of infants
- Furunculosis
- Carunculosis
- Oriental sore.

B. Diseases Caused by Bacilli
- Diphtheria of the skin
- Anthrax
- Glanders
- Lepra
- Tuberculosis of the skin
  - Lupus vulgaris
  - Scrofuloderma
  - Erythema induratum
  - Tuberculosus cutis orificialis (tuberculous ulcers)
  - Tuberculosis verrucosa cutis
  - Acute tuberculosis in children
  - Exanthematous miliary tuberculosis
- Tuberculid
  - Lichen scrofulosorum
  - Acnitis
  - Folliclis
  - Acne scrofulosorum.

C. Diseases Caused by Spirilli
- Syphilis
- Frambesia.

D. Diseases Caused by Vegetable Parasites
- Favus
- Tricophytosis
  - Trichophytosis capitis
  - Tinea kerion
  - Trichophytosis corporis
- Eczema marginatum
  - Eczematoid ringworm of the extremities
- Tinea versicolor

- Tinea Imbricata
- Pinta
- Actinomycosis
- Blastomycosis
- Sporotrichosis.

E. Diseases Caused by Animal Parasites
- Scabies
- Pediculosis
  - Pediculosis capitis
  - Pediculosis corporis
  - Pediculosis palpebrarum
- Grain itch
- Ixodes
- Brown tail moth
- Pulex irritans
- Uncinarial dermatitis
- Creeping eruption
- Craw Craw
- Cimex lectularius.

CLASS III: Artificial Dermatoses (known etiology)
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  - Dermatitis ambustiones
  - Dermatitis congelationis
- Dermatitis venenata
- Dermatitis traumatica
- Dermatitis factitia
- Radiodermatitis, Radium dermatitis
- Dermatitis medicamentosa
- Serum eruptions.

CLASS IV: Diseases of Unknown Etiology.
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- Napkin erythema (erythema of Jacquet)
- Pernio
- Erythema scarlatiniforme
- Erythema intertrigo
- Erythema multiforme
- Erythema nodosum
- Urticaria
- Lichen urticatus
- Angioneurotic edema
- Prurigo
- Urticaria pigmentosa
- Hydroa vacciniforme
- Hydroa puerorum
- Lichen planus
- Lichen spinulosus
- Pityriasis rubra pilaris
- Pityriasis rosea
- Psoriasis
- Parapsoriasis
- Herpes simplex
- Herpes zoster
- Pompholyx
- Pemphigus
- Pemphigus acutus
- Pemphigus vulgaris
- Pemphigus foliaceus

Pemphigus vegetans
Dermatitis herpetiformis
Eczema
Granuloma annulare
Dermatitis repens.

CLASS V: Hypertrophies, Atrophies, Neuroses and Anomalies of Pigmentation.

A. Hypertrophies
  Clavus
  Callositas
  Keratosis pilaris
  Keratosis follicularis contagiosa
  Lichen pilaris seu spinulosus (Crocker)
  Verruca
  Verruca planum juvenilis
  Verruca plantaris
  Cornu cutaneum
  Porokeratosis
  Acanthosis nigricans
  Angiokeratoma
  Scleroderma
  Morphea
  Morphea guttata
  Dermatolysis.
B. Atrophies and Neuroses
  Ainhum
  Pruritus
  Pruritus hiemalis
  Tricotillomania.
C. Pigmentary Disorders
  Lentigo
  Chloasma
  Vitiligo.

CLASS VI: Acquired New Growths of the Skin.

Cicatrix
Keloid
Lipoma
Telangiectasis
Angioma serpiginosum
Granuloma pyogenicum
Molluscum contagiosum
Sarcoma.

CLASS VII: Diseases of the Appendages of the Skin.

A. Diseases of the Coil Glands
  Hyperidrosis
  Anidrosis
  Bromodrosis
  Chromidrosis
  Hematidrosis
  Uridrosis
  Sudamen
  Miliaria rubra
  Granulosis rubra nasi.
B. Diseases of the Sebaceous Glands
  Seborrhea
  Dermatitis seborrhoica
  Pityriasis capitis

- Pityriasis simplex
- Pityriasis steatoides
- Comedo
  - Grouped comedones in infants
- Acne vulgaris neonatorum.

C. Diseases of the Hair and Hair Follicles
- Atrophia pilorum propria
  - Fragilitas crinium
  - Monilethrix
  - Trichorrhexis nodosa
- Canities
  - Ringed hair
- Alopecia symptomatica
- Alopecia areata.

D. Diseases of the Nails
- Atrophia unguium
  - Anonychia
- Onychomadesis
- Onychoschizia
- Koilonychia
- Grooved nails
- Leukonychia
- Onychauxis
- Pterygium
- Onychia
- Paronychia
- Ungius incarnatus
- Eczema of the nails
- Psoriasis of the nails
- Syphilis of the nails
- Onychomycosis.

E. Diseases of the Mucous Membranes
- Transitory benign plaques of the tongue (wandering rash)
- Glossy plaques
- Leukoplakia
- Perleche
- Furrowed tongue
- Black tongue
- Cheilitis glandularis
- Cheilitis exfoliativa
- Fordyce's disease
- Periadenitis mucosa necrotica recurrens
- Intra-oral herpes
- Bednar's aphthæ.

CLASS I. AFFECTIONS OF CONGENITAL ORIGIN

(A) Superficial Congenital Affections

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Ichthyosis.—Definition.—A chronic congenital cutaneous affection of various types, characterized by a more or less generalized dryness and scaliness, and sometimes associated with keratotic or verrucous follicular papulation.

Under this title, commonly spoken of also as fish-skin disease or xeroderma, are included ichthyosis simplex (xeroderma or true ichthyosis), ichthyosis congenita or harlequin fetus, and ichthyosis hystrix.

Symptoms.—Ichthyosis simplex is usually first noticed within the first two years after birth. In its mildest form it is known as xeroderma or xerosis, in which instance the skin generally or only that of the extensor surface of the trunk and extremities is dry, rough, and scaly. The scales are "branny" and easily brushed off. The process is most pronounced during the colder months and frequently is associated with a varying degree of keratosis pilaris, which is most marked on the posterolateral surface of the arms and the anterolateral surface of the thighs. Usually, also, the skin of the extensor surface of the elbows and knees is thickened. The condition usually progresses until adult age is reached, the scaling becoming more pronounced, and it varies within certain limits depending upon the climate.

These facts hold true for ichthyosis simplex in its more marked form, the so-called true ichthyosis, but in this the condition is generalized and the scales are of a gray, coarse, plate-like character, usually quadrilateral or diamond-shaped. In this form, the epidermis may be slightly thickened and its cleavage lines exaggerated. The scales are attached at their centers and their free margins tend to curl upward. The scalp is dry and scaly and the hair lusterless. The nails are usually brittle and easily broken.

In true ichthyosis the skin assumes the appearance of that of a fish or alligator. Because of the loss of elasticity, mobility may be interfered with and fissures may form on the surfaces over the joints. Eczematous complications, most frequent on the face, are not uncommon. Ordinarily, subjective sensations are absent. The sweat and oil secretions are much diminished or apparently absent.

Ichthyosis congenita or "harlequin fetus" is a condition rarely observed, one in which the infant, which often is prematurely born, dead or alive, is covered with coarse epidermic plates, usually greasy and separated from each other by furrows so deep as to extend down into the corium. The monster is usually without ears, nose, eyelids, or lips, these being replaced by corneous folds, and the fingers and toes have been likened to talons. These cases, if not stillborn, usually perish within a few days or weeks through inability to nurse. There is a similar condition which does not affect the general health of the patient, that is, a delayed physiologic shedding and which soon terminates either in a complete recovery or as an ordinary persistent ichthyosis.

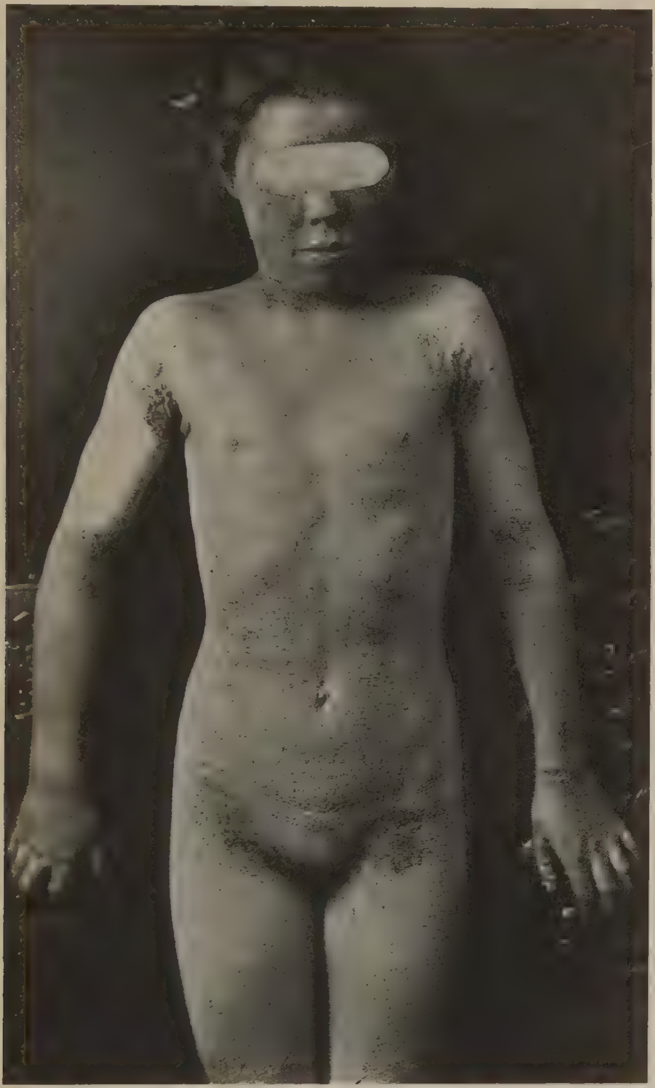

Fig. 1.—Ichthyosis. Girl of 12 years. (Collection of Dr. Grover W. Wende.)

Ichthyosis Hystrix.—This condition closely simulates certain types of nevi and is not regarded as a variety of ichthyosis by many authors. The lesions consist of circumscribed, dry, rough, yellow-gray or greenish patches of corneous or verrucous elevations and spines, usually but few patches in all, but may be so extensive as to occupy a large proportion of the body surface. The disease may occur alone or in association with ichthyosis simplex.

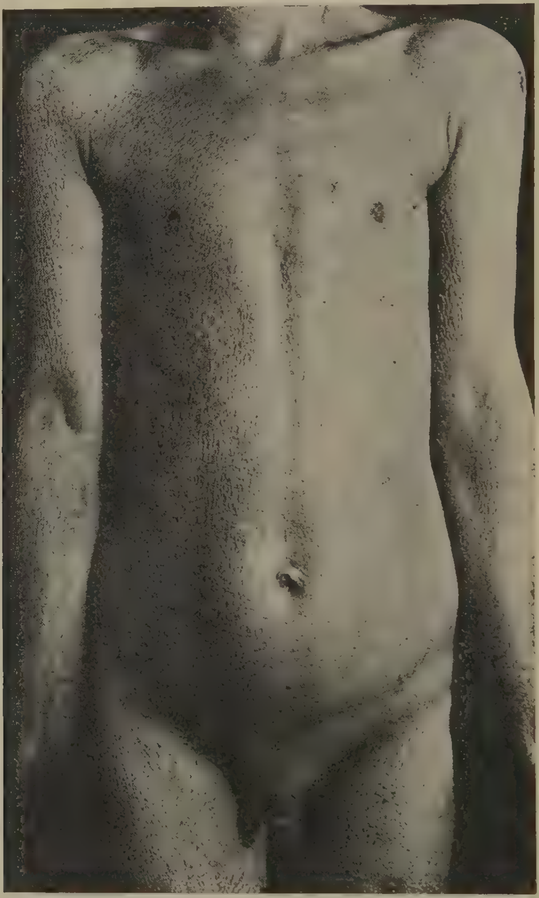

FIG. 2.—Ichthyosis. (Fordyce and MacKee.)

Etiology.—Ichthyosis is congenital but as a rule does not become manifest until the end of the first year. The majority of the cases are with hereditary factors. Males and females are affected about equally.

Pathology.—The rete is atrophic and the corneous layer is hypertrophic. The cells of the latter are without nuclear fragments, due to an atypical process of cornification as yet not understood. The extremities of the rete pegs and papillæ are described as being broad and flattened and of a dove-tailed appearance. The vessels of the corium are sometimes dilated. The epithelium of the coil glands is swollen and these glands are dilated.

Diagnosis.—This scaling anomaly is differentiated from all others by its classical history and the absence of all signs of inflammation. An eczematous condition is sometimes superimposed but this can be recognized by the presence of characteristic scaling also on the non-inflamed portion of the integument. Ichthyosis hystrix should not be confused with linear nevus.

Treatment.—Internally, extract of thyroid is sometimes of value. Hypodermic injections of pilocarpin (gr. ¼) may be of some benefit by producing an increase in the oil and sweat supply to the skin.

Warm alkaline or vaporous baths followed by the use of simple oily preparations, such as one part of glycerin to three of olive oil, usually will control successfully the simple cases. The free use of sapo viridis with hot baths is recommended for removal of the scaliness in severe cases. In the more severe types, for keeping the skin soft and pliable, a keratolytic agent such as salicylic acid should be added to the oily lotion or ointment. Almond, linseed or cocoanut oil are often employed in the lotions. Benzoinated lard, lanolin or eucerin are used most commonly, either alone or with 1 to 5 per cent, of salicylic acid, as ointment bases. Severe hystrix lesions may be removed by excision; caustics are hardly to be recommended.

Prognosis.—Although the general health is unaffected, the disorder always remains throughout life. Two exceptions have been reported. Much relief may be obtained by persistent proper therapeutic measures. Change of climate is often of value. Those affected are usually better in hot weather and moist atmosphere.

Erythrodermie Congenitale Ichthyosiforme.—Definition.—A congenital generalized erythema associated with or soon followed by permanent scaliness which is most marked on the flexor surfaces.

Symptoms.—In nearly all of the few reported instances, the disorder was first recognized at birth as a generalized redness which was soon followed by scaling similar to that observed in ichthyosis. The scaling has been reported also as preceding the erythema. When the erythema diappears, which it usually does in the course of a few weeks or months, an atypical ichthyosis remains, atypical in that the flexor surfaces are most markedly involved. The severity of the erythema as well as of the scaling and thickening is variable. The thickening may become of the "hystrix" type in patches. There is usually a hyperkeratosis of the palms and soles and the scalp hair and the nails have been reported as having a tendency to rapid growth. Bullous lesions are also recorded as occurring on the extremities. Perspiration is said to be limited except on the palms and soles and flexor surfaces of the extremities. Mild itching may occur or there may be no subjective or systemic disturbances.

Etiology.—The cause of the disorder is obscure.

Pathology.—The microscopic picture is altogether that of a hyperkeratosis together with a slight chronic inflammatory process in the papillary corium.

Diagnosis.—The erythema and its predilection for flexor surfaces should aid in its differentiation from ichthyosis.

Treatment.—The treatment is essentially the same as that for ichthyosis and keratoderma.

Prognosis.—The disorder persists, usually as an ordinary ichthyosis.

Keratolysis.—Under this title, or that of *deciduous skin*, are included the few reported cases of periodic shedding of the skin.

Some observers relate it, clinically at least, to relapsing erythema scarlatiniforme, but the etiology and pathology are not understood.

The individuals affected shed their skin at approximately or entirely definite intervals, as do serpents. Cases have been reported which shed once in 365 days; others twice yearly, etc. The shedding occurs in large sheets and is usually preceded by constitutional symptoms, ordinarily mild, consisting of fever, nausea and vomiting, weakness, headache, and general malaise. The premonitory skin symptoms consist of dryness, heat, and slight or no erythema. The mucous membranes and nails also may be affected. The disorder may be first noticed shortly after birth or it may begin during the first decade of life or even later, and apparently continues throughout life. The actual shedding process usually begins within two or three days after the onset of the constitutional disturbance and requires from three days to three weeks for its completion.

Keratodermia Palmaris et Plantaris.—Definition.—An hereditary or acquired, sometime congenital, symmetrical, partial or complete thickening of the horny layer of either the palms or soles, usually both.

Symptoms.—The condition is practically always acquired but frequently shows an hereditary history. The congenital variety is unusual and begins within a few weeks of birth as a scaling and gradual thickening of the palms and soles, later either becoming warty or resembling the acquired type. In the common variety, the skin becomes a hard epidermic plate, smooth, translucent or opaque, yellow-brown, and averaging an eighth of an inch or more in thickness. A verrucous or "worm-eaten" appearance is sometimes noted. The condition rarely passes beyond the sides but sometimes extends a short distance on the dorsum of the hands or feet, especially over the knuckles. The thickening may be localized or diffuse. The sites of ordinary calluses, the result of friction and pressure, are first and most markedly involved. The arch of the sole is usually only slightly affected or is uninvolved, the process being most pronounced on the heel and ball of the foot. The distal ends of the nails are sometimes tilted upwards by the thickening and hardening beneath their free borders, and they, too, sometimes become thickened and altered in color. Infrequently, because of an associated hyperidrosis, which is most common in the acquired cases, the hypertrophy is of a sodden character. Ordinarily, the thickening is not uniform, being greatest at the sites mentioned, and with only slight or moderate overgrowth of the intervening integument. The condition, even in the absence of treatment, often varies as to severity, periodically becoming much less marked or clearing entirely; however, only to recur. As a rule it remains practically stationary. Uncommonly it is associated with inflammation, especially at its periphery and this also is more or less transitory. Subjective symptoms are, as a rule, lacking, but slight tenderness as well as discomfort from fissures may be present.

Etiology.—Friction and pressure apparently are sometimes exciting causes. That there is a definite hereditary factor in a large proportion of the cases there can be no doubt; it is frequently traced back through several generations, one or more occurring in each generation, the condition showing a tendency to affect largely or entirely one sex.

Pathology.—This histologic picture in all essentials is similar to that of callositas, a thickening and hardening of the corneous layer being associated with a marked acanthosis. The oil glands are often hypertrophied.

Diagnosis.—Keratoses, the result of arsenic ingestion, a chronic eczema of the parts, and squamous syphilids, as well as occupational callosities, are differentiated from the acquired type without difficulty. The congenital variety resembles a condition spoken of as *mal de meleda*, a congenital hereditary palmar and plantar keratosis which may affect other parts also and which is an endemic disease of the Island of Meleda.

Treatment.—Arsenic internally is of value, and may be given in any form to adults. Keratoses due to arsenic are, of course, improved upon withdrawal of this drug. It is usually administered in increasing dosage in the form of liquor arsenicalis, Fowler's solution, or the Asiatic pill. For both the congenital and acquired varieties of keratoderma, a keratolytic agent, perferably salicylic acid in from 3 to 5 per cent. strength in equal parts of lanolin and petrolatum, with or without the addition of from 5 to 10 per cent. of ammoniated mercury, is of greatest benefit. Salicylic acid plasters also are worthy of mention for use in marked cases. The tincture of green soap may well be used morning and evening as a shampoo on the parts. Roentgenotherapy in proper dosage is of unquestionable merit in most cases.

Prognosis.—The inherited variety usually persists throughout life, and although without annoying subjective sensations, interferes with duties requiring delicate usage of the hands. By constant treatment the parts can be kept fairly soft and pliable. The acquired form is more amenable to treatment, permanent relief being reported in many instances.

Milium Congenitale (En Plaques).—Under this title Crocker described two cases of a special variety of milium, which, since, has been observed by only a few other individuals. The lesions are present at birth and occur on the scalp and face as reddish or pale red-yellow, well-defined patches of closely aggregated, yellow, pinpoint sized papules, giving the surface a finely granular appearance. The patch is slightly raised above the surrounding skin, and this characteristic is most marked at the periphery, where the papules are most distinct and where comedones are in greatest numbers. There are few or no hairs in the involved area when present in the scalp. No change after birth has been noticed.

Etiology.—Crocker believes the lesions to be constituted of milia, the result of miscarried embryonic epithelium, as described by A. R. Robinson. He also suggests, as the exciting cause, an adherence of the amnion at an early stage of fetal life, possibly from a deep-seated intra-uterine inflammation.

Pathology.—The structure is composed of nucleated epithelial cells inclosed in a fibrous pseudo-capsule and situated in the papillary portion of the corium.

Treatment.—Excision is recommended if the lesion is small enough to allow primary union.

Congenital Hirsuties.—**Definition.**—Abnormal hairiness of the newborn.

Symptoms.—Congenital hirsuties may be partial or general. Both anomalies are rare, but the former is more often encountered. It is observed as a hypertrichosis of parts normally devoid of hair and, as a rule, constitues an illustration of the hairy nevus. These areas vary greatly in size, color, and elevation and the hairs in them may be long or short, course or fine, and numerous or sparse. It is, therefore, usually the seat of a hyper-pigmentation and increased connective tissue formation and is most commonly situated on the lower portion of the trunk behind, sometimes in association with a spina bifida. The general or universal variety is a hairy overgrowth of all parts of the body normally provided with hair, the palms and soles, therefore, being unaffected. It is most marked on those parts where hair-growth normally is greatest, the scalp being the most evident seat. The lanugo hairs appear as down at or shortly after birth, growing appreciably within a few days, weeks or months, and, at the same time, usually assuming more preceptibly the hue of the scalp hair. The degree of the pilosis may vary from the scarcely noticeable to the very conspicuous.

Etiology.—The cause of the partial form, as of all nevi is unknown. Whatever may have caused the increased blood supply to the affected area is probably a factor. Although the direct cause of the universal cases is not understood, frequently, in these cases, there is a hereditary tendency. This latter type is usually in males and is associated not uncommonly with congenital defects, as, for instance, abnormal tooth development, which rather frequently accompanies it. Races in which dark, coarse hair is a characteristic and individuals of dark complexion are generally those universally affected.

Prognosis.—There is a possibility that the partial form, if associated with true nevus formation, may become more extensive, but this is not the rule. It is possible to remove these hairs but practicable only if the lesion is small and in a disfiguring locality. The universal variety tends to become more in evidence with age but none other than cosmetic disfigurement results. There is no remedy for this condition.

Treatment.—If the partial variety occurs as a nevus, pigmented or unpigmented, it should be treated as such. This is practicable only, as previously stated, in inextensive cases occurring on portions of the body usually exposed. The hairs can be removed permanently by electrolysis at the hands of an expert, but because of the time element necessary for such removal cases of universal distribution cannot be treated, even for the cosmetic results to be obtained from the removal of the facial hairs alone.

Alopecia Congenita.—**Definition.**—Alopecia congenita implies a partial or universal, temporary or permanent, natal or post-natal, absence of hair.

Symptoms.—This condition is to be regarded as an anomaly rather than as a disease. All forms are very uncommon.

The partial variety may be localized or general in distribution. In the localized cases there may be either a *total* or an *incomplete* alopecia in circumscribed areas of various sizes. By "incomplete" is meant either a general scantiness of hair or a lack of development as regards length or breadth of the hairs of these areas. The partial cases of generalized distribution include both the changes mentioned as occurring in the localized variety, the only difference being that the patches occur here and there on all parts of the body. To this class also belong those cases in which there is a general thinning of the hair of the entire body-surface.

The universal variety, denoting a complete absence of body-hair, may be present at birth or may occur within a few weeks after. When all hair is absent at birth, hair-growth never takes place. In these cases, there is a cessation of development of the hair-follicles at various stages of embryonic growth and the mouths of the hair-follicles are absent. Not even the rudiments of the hair-follicles have been demonstrable in some of the cases. In the type of the universal variety in which the hair is shed shortly after birth, spoken of as universal congenital hypotrichiasis, the hair in gross is primarily normal in length, breadth, and color but the regrowth is never normal, persisting in the form of scanty down or sparse hair of otherwise impaired vigor. There also is a class of the universal variety in which hair-growth is simply retarded for the first year or two.

Associated anomalies have been reported in a large percentage of cases of congenital alopecia, such as defective development in the size, shape and number of the teeth, alteration of the nails, webbing of the fingers and toes, and atrophy of the tips of the fingers. The tooth and nail changes are by far the most common and occur most frequently with the permanent congenital universal variety. Retinal changes have been reported, as have been certain diseases, notably epidermolysis bullosa, xeroderma, and alopecia areata.

Etiology.—Heredity is the most commonly recognized factor and is illustrated in both the natal and post-natal groups. Certain races have a tendency to more scanty hair-growth than others. Some of the cases mentioned in the literature have occurred in families of close intermarriage. About two males are affected to every female. Most of the persistent cases are those of congenital universal distribution, the hair-follicles being absent due to embryonic cessation of growth.

Pathology.—The microscopic examination of the cases in which the entire body is devoid of hair at birth may show either an arrested growth of the hair-follicles at any stage of development or their complete absence. In the latter case none of the rudiments are demonstrable and there are no hair-follicle openings on the skin. In one of these cases all of the sebaceous glands opened directly on the skin. The former condition is more common and usually corresponds to the external root-sheath.

Two observers have reported the epidermis as atrophic and the corium replaced by "cord-like areolar growth." Various embryonic stages of activity are noted in the hair-follicles in those cases in which there is alteration of growth at birth but later normal or approximately normal hair develops, simply more time than normal being required for the development.

Prognosis.—The prognosis is extremely unfavorable, especially in the presence of an hereditary element. In the cases in which the hair-follicle development has been completely arrested, there is, of course, no hope of growth. In the other varieties rare exceptions do occur, normal or slightly altered growth finally taking place.

Treatment.—The treatment, excepting for special regard to any etiologic factors that can be elicited, is that for simple alopecia, as mentioned elsewhere.

Albinism.—**Definition.**—A congenital and permanent universal absence of pigment in the skin, hair, irids, and choroid.

Symptoms.—Albinos, the term applied to subjects of albinism, have milky-white skin, usually with a pinkish tinge due to the integumentary blood supply, white or yellow-white, silky, fine hair, colorless, pinkish, or pale blue irids, and the pupils, because of absence of pigment in the choroid, are red or pink. The subjects of the disorder may show various degrees of photophobia and nystagmus, the resistance to light being lessened by the absence of pigment in the eyes. Not infrequently myopia is encountered in these individuals. The skin is of normal structure and function except for the pigment anomaly. Although considered as a permanent affection, the pigment is reported as having partially returned in three or four instances. Those affected not uncommonly are deficient mentally or physically.

Etiology.—Albinism is most frequent in negroes and other races characterized by heavily pigmented skin. It is now thought to be due to faulty development of the pigment-producing apparatus, probably due to the lack of a ferment which is needed to cause the excretion of pigment. Consanguinity and inheritance are important factors. Often several children of a family are affected. Because of the fact that it is unusual to find albinos in two succeeding generations and because of its frequency in the offspring of related parents, especially first cousins, it is classed by some, in terms of Mendelian theory, under the recessive type of inheritance. The disorder is illustrated in the lower animals, as for instance, the albino rabbit, and also occurs in the bird, fish and plant kingdoms.

Treatment.—The condition is without remedy.

Xeroderma Pigmentosum.—Definition.—Xeroderma pigmentosum is a chronic, malignant, cutaneous symptom-complex of children, occurring chiefly on the exposed surfaces of the body, beginning as freckle-like areas of pigmentation, and followed by atrophic patches, telangiectases, verrucous and epitheliomatous tumors, and a fatal termination.

Symptoms.—The disease usually begins within the first year of life, but has been reported in exceptional instances as first observed in adults, even of advanced years. It is questionable whether the cases first observed in adults are related to the condition seen in infants. It is first noticed as hyperpigmentation in the form of pin-head to large pea-sized, isolated, round or irregular, freckle-like macules of the face, neck, ears, hands, forearms, and upper chest in front and behind. With the progression of the disease, involvement of the upper arms, portions of the lower extremities and trunk, the scalp and the mucous membranes of the conjunctiva, lips and tongue is not uncommon. On the extremities, the extensor surfaces are predilected, although sometimes even the palms are affected. Several observers have noted that the hyperpigmentation is preceded for several days by diffuse or patchy erythema and scaling. Most cases begin in summer following exposure to the sun's rays. The lentigenes may disappear in cold weather for the first year or two but then they become permanent, growing darker with age and displaying a tendency to increase in number and size, sometimes coalescing to form large patches. Coincidently with or shortly after the onset of this pigmentation, telangiectases and permanent, white, atrophic spots appear on the hands and face, and later on other portions of the body. The atrophic areas become more and more numerous, sometimes coalescing into large patches, and may be present either upon otherwise uninvolved skin or upon hyperpigmented lesions as smooth and glistening or wrinkled, dry areas, sometimes finely scaly. The telangiectases may be punctate, linear, or stellate, and they occur chiefly in or at the peripheries of the atrophic areas; sometimes they are elevated in the form of small angiomata, especially in the later years of the affection. After a variable period of months or years with the disease persisting and progressing as above described, the more formidable stage is reached, consisting of new growths which develop upon the areas of hyperpigmentation, at first largely keratotic and verruciform, later, interspersed with epitheliomatous and sarcomatous lesions which have developed from them, the edges of the nose and ears being favorite sites. These tumors have a marked tendency to ulceration.

In the later stages the atrophy is usually responsible for many disfiguring cicatricial contractions, especially about the nose, eyes, and lips. Ectropion is sometimes associated with fissures and ulcers of the lips, conjunctivitis, pterygium, pinguecula, corneal opacities and ulcers, and tumor-growths of the eye.

Subjective symptoms at first are either absent or occur in the form of general depression following a period of marked stimulation. Lacrimation photophobia and impairment of vision are often observed even early in the disorder, the eyes being noted in some cases to be the first part affected. Lessened sensibility and decreased activity of the sweat-glands occur in the atrophic areas. The general health of the patient is apparently unaffected until during the later stages of the disorder when marasmus, pain, cachexia, and exhaustion accompany the malignant ulcerative formations, finally bringing about death.

Etiology.—The cause of this rare disorder is unknown but there are several fairly definite factors. It is a disease of early life. There is unquestionably an inherited peculiarity that makes one susceptible, for frequently the disease is cited as occurring in several children of a family. Males and females are about equally affected but the cases in any given family are usually limited to one sex. Most cases begin in the summer or following exposure to the sun. Consanguinity is not infrequently a factor. About one-fourth of the cases reported have occurred in Jews.

Pathology.—The disease, *per se*, is one of the cutaneous system, malignancy of the internal organs being very exceptional. The microscopic pathology of the disorder is in no way unique, the various changes noted being essentially the same as those observed in lentigenous pigmentation, atrophic spots, telangiectases, verrucæ, tumors of various sorts, and ulcerations respectively. The tumors are either entirely epitheliomatous, as is the rule, or of a mixed type consisting of a predominence of epitheliomatous tissue in the presence of granulomatous, sarcomatous, myxomatous, and angiomatous changes. The ulcers are usually purely the result of broken-down malignant growth but they may be pyogenic in origin.

Diagnosis.—The malady is readily recognized after the production of any of the lesions which follow the hyperpigmentation; the freckle-like spots alone, however, may easily escape suspicion. Early atrophic patches of scleroderma, associated with pigmentation, sclerosis, and telangiectases, might be confounded temporarily with this disease, but the areas involved are of different location and, in the former, the atrophic patches are firm, rather than soft, pliable and scaly. In scleroderma there are larger and more irregular areas of pigmentation and a characteristic leather-like induration. Keratosis senilis with degenerative plaques, seen on the face and hands of elderly people who have been much exposed to the sun, might be mistaken for xeroderma pigmentosum as seen in the aged. In both, epithelioma is a common sequence.

Prognosis.—Death is almost inevitable and usually the result of the cancerous lesions. The child may die of marasmus within a few months of the onset of the disorder or may live to young adult age and then succumb to cachexia.

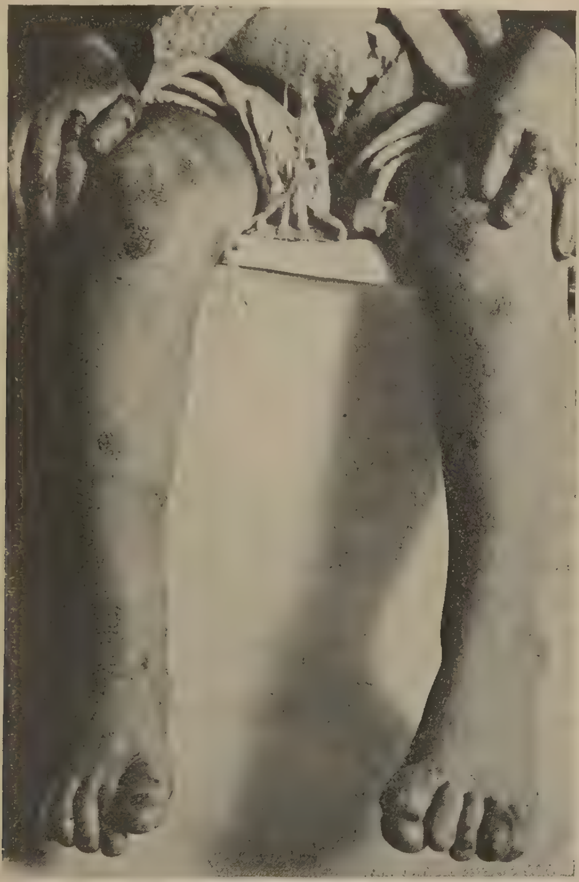

FIG. 3.—Epidermolysis bullosa. (Fordyce and MacKee.)

Treatment.—This is highly unsatisfactory. No internal medication has proved of noteworthy avail. Autogenous serums have been reported as used to some benefit. Proper hygienic conditions should be strictly observed. The *x*-ray and carbon dioxid snow are of value in the removal of the tumors, and the former has been reported as apparently curative of xeroderma pigmentosum in several instances. The ulcers and new-growths may also be removed by surgical measures, such as curettage and excision. Eye symptoms require special management but a boric acid and borax wash frequently used is always of advantage. The patient should be protected from the sun and wind.

Epidermolysis Bullosa Hereditaria.—Definition.—An exceedingly rare, congenital tendency to vesicle and bulla formation of any part of the integument subjected to any form or degree of traumatism.

Symptoms.—Large or small tense bullæ, usually containing clear or amber fluid, rarely hemorrhagic, appear within a few hours on parts subjected to pressure, friction, bruising, or other traumatism of varying degree. This tendency usually becomes manifested within the first two years of life, although a few instances have been noticed first in adult years and have been considered a similar process. The lesions of the ordinary variety may occur on any part of the body but are most frequent on parts constantly subjected to friction and pressure, such as the collar and waist regions, the hands and feet, the shoulders, and the extensor surface of the joints, notably the elbows and knees. In what is spoken of as the dystrophic form, atrophy and less transitory pigmentation result in the involved areas and the lesions are more frequently hemorrhagic. Here, also, occurrence on the buccal mucosa is less foreign. Malformation of the nails is not unusual and atrophy of the digits is reported as a common sequel. Milia, frequently grouped, have been noted by several observers as being most numerous on the parts most commonly affected. The bullæ remain several days, disappearing after rupture or partial absorption. The lesions are usually somewhat painful, especially after rupture, and sometimes there is an associated itching or burning or both.

The general health of the patient is unaltered and the skin in gross remains normal so long as it is not subjected to trauma.

Etiology.—The malady is decidedly of hereditary character, most of the cases, with the exception of the few illustrations of the acquired form, giving a history of occurrence in one or several of the offspring for several generations. As mentioned, trauma is the exciting cause. As yet, no other factors are accepted. That the disorder is an angioneurosis of hereditary origin is perhaps the most logical explanation.

Pathology.—The bullæ are situated deep in the rete, or between it and the true skin, and the papillary vessels are greatly dilated, according to Elliot. Perivascular cellular infiltration he found limited to the subpapillary cutis. In each of four cases Engman and Mook found the elastic tissue of the corium diminished or absent. This has been confirmed by others.

Diagnosis.—Rarely, the disorder is confused with pemphigus, but in the latter the lesions appear spontaneously and without congenital character.

Treatment.—A mild antiseptic ointment should be used to protect the raw surfaces of evacuated blebs. Strict avoidance of irritation to the skin, purely a prophylactic measure, is of greatest importance.

Prognosis.—The condition usually continues throughout a lifetime, although frequently with advancing years the tendency becomes less pronounced.

Edema Neonatorum.—Synonym.—Sclerema edematosum.

Definition.—Edema neonatorum is a symptom of a disease, rather than an entity in itself, characterized by a general anasarca, most marked in the lower extremities and dependent parts of the body, in premature infants with impaired circulation, usually resulting in the death of the fetus or infant before, during, or very soon after birth.

Symptoms.—This condition may be present at birth even in a dead fetus, but more commonly develops within the first two or three days. The cutaneous swelling may be partial, but is, in rare instances, complete. It begins almost invariably in the lower extremities, the dependent parts of the thighs often first involved. It then gradually and almost simultaneously involves the remainder of the lower limbs and dependent portions of the trunk and upper extremities. The swelling is marked in the lax tissues of the eyelids, scrotum, and labia majora, and remains soft here, but the dependent parts of the body elsewhere may become so hard as to be truly indurated. The skin pits under pressure and is colder than normal. The color is pale, dirty-yellow, slightly livid or light brown. Drowsiness, usually preceding the onset in the cases which begin after birth, becomes more and more intense with the progression of the disorder, the infant often soon passing into coma. The body temperature is usually somewhat subnormal, the circulation weak, and the respirations shallow. These factors become intensified from day to day, the cry becoming weaker and weaker, death ensuing within four to six days with an associated intercurrent pulmonary or cardiac disorder, not infrequently preceded by convulsions and diarrhea. The urine characteristics of edema are obtainable.

Etiology.—The disorder usually occurs in the premature offspring of ill-nourished mothers. Chilling of the infant and imperfect establishmlent of respiration at delivery also predispose. Vitality impaired by associated renal, cardiac, and pulmonary disease or defect, not unlike the causes of anasarca in the adult, as a rule is responsible for the affection. Schumann divides the 106 cases in the literature collected by him in 1915, into two groups: (1) Those due to some mechanical or structural defect in the fetus or its membranes, and (2) those due to toxemia of the mother and secondarily of the fetus, without any morpologic defect necessarily present.

Pathology.—Apart from the associated etiologic pathology hinted at above, as for instance, nephritis, pulmonary atelectasis, venous thrombosis, cardiac anomalies, etc., the general hydrops is often evidenced by serous transudation into the pleural, pericardial, and peritoneal sacs, by moderate internal hydrocephalus, and usually by edema of the placenta. In the cutaneous system there is marked serous effusion, more especially in the reticular portion of the corium and interstices of the subcutaneous tissue. This process is also of varying degree in the underlying muscles. The skin is reported as not normally developed, but corresponding microscopically to that of a six to eight months fetus.

Diagnosis.—Sclerema neonatorum and scleroderma neonatorum are to be differentiated; the former, as described under that disorder. Scleroderma neonatorum is of later appearance in the infant, is rarely of equal extent, does not tend to affect the dependent portions of the body, is usually unassociated with recognizable disease of other organs, the pulse, temperature, and respiration are unaffected, pitting under pressure is less pronounced, and there is no tendency to a rapid and fatal termination.

Prognosis.—About 90 per cent. of all cases perish, those surviving being affected only to a limited extent and being without serious causative or intercurrent disorders.

Treatment.—Treatment is essentially that of sclerema neonatorum plus that of any disease causing or complicating the edema.

Sclerema Neonatorum.—**Synonym.**—Sclerema adiposum.

Definition.—Sclerema neonatorum is a comparatively rare, rapidly progressive, indurative condition of the skin and adjacent tissues of weakly infants, which begins in the lower extremities or the lumbo-sacral region, involving the entire integument saving the palms, soles, eyelids, scrotum, labia majora and chest in front and which is associated usually with subnormal temperature and a fatal termination.

Symptoms.—This morbid disorder may be present at birth but usually begins within the first two or three days, rarely after the tenth, its progression usually being completed within three to five days. It is first noticed, as a rule, in the lower limbs or lower trunk posterior, as an ivory-yellow, wax-colored induration, oftimes later becoming livid. The involved area at first is more easily palpable than visible, the variation from the general color of the sickly infant being slight and there being little or no swelling. Its symmetrical spread is rapid to the trunk, upper extremities, and head, no part of the skin being unaffected excepting that of the palms and soles, the lax tissues of the eyelids, scrotum, and labia majora, and, in some instances, the front of the chest. The process is always most marked in the dorsum of the trunk and extremities. The skin finally becomes immovable, apparently firmly attached to the subcutaneous tissue, as seems the latter also to the underlying muscle and bone. The skin, though without swelling, appears very tense in the marked stages, its normal lines being effaced, and it is dry, shiny, and "leathery." There is no appreciable pitting following pressure. The body assumes a state of cadaveric rigidity, having a "frozen" appearance, the joints "fixed" to active or passive motion, the opening of the mouth and deglutition becoming impossible. The surface of the body feels cold and of about the consistency of suet. The temperature is practically always subnormal; in cases on record it is reported as low as 72°F., although in rare instances pyrexia has been reported. The pulse and respiration are weak and slow.

The disease may be found with or without the association of other recognizable morbid conditions, the cases which begin as late as the first or second month of life usually being ushered in and associated with pulmonary, cardiac, and gastro-intestinal disturbances. Extreme prostration, convulsions, paralyses, diarrhea, icterus, bronchitis, bronchopneumonia, edema of the vocal cords and glottis, and aural thrush are all reported but usually as secondary to sclerema.

Etiology.—The cause of the disease is unknown. It is seen most commonly in emaciated infants in foundling houses and similar institutions. In the cases present at or very shortly after birth, immaturity, congenital weakness, congenital lues, illegitimacy, parental poverty, maternal debility, occurrence of birth in very cold surroundings, and cardiac and pulmonary anomalies are cited as factors. In the cases that develop somewhat later, cholera infantum, pneumonia, etc., seem to be exciting causes. Attention has been called to the similarity of the lesions of sclerema to those found in certain of the trophoneuroses. In myxedema there is an induration which does not pit upon pressure, one of the chief reasons for believing sclerema neonatorum an endocrine gland derangement. Other observers regard microbic infection as the best explanation of this kind of toxemia.

Pathology.—Besides the gross and associated pathology as previously mentioned, visceral changes may occur as complications, in the form of inflammations and hemorrhages, and transudations and hemorrhages into the serous cavities have been reported as unconstant findings. The skin cuts like cutting bacon rind and the subcutaneous fat is white. The skin and body-tissues are very dry, probably brought about by the diarrhea present in most cases. Chemically, a relative increase of the fats of higher melting points, stearin and palmitin, is found to be normally present in the fat-content of infants, the fat of low melting point, olein, being relatively decreased. This factor, because of the decrease in body temperature, is regarded by some to be responsible for the congelation. *Histologically*, there is a subcutaneous infiltration with "small cells" and an increased fibrosis with atrophy of the adipose tissue. There is very little fat in the cells and they are shrivelled and with distinct nuclei. The adipose tissue contains an abundance of fatty acid crystals. The rete and corium are very thin and their cells are indistinct. The papillary vessels are contracted. The stratum corneum is unchanged.

Diagnosis.—This entity must be differentiated from edema neonatorum, scleroderma neonatorum, tetanus neonatorum, and erysipelas neonatorum. In edema neonatorum, which is the most likely error in the diagnosis, the joints, including the jaws, are mobile; there is swelling of the integument, well marked in the loose tissues of the eyelids, scrotum, and labia majora; there is no marked induration but a definite pitting upon pressure; and there usually is associated a recognizable renal, cardio-vascular, or other contributing etiologic lesion. In scleroderma of infants there is no tendency to a rapidly fatal termination; the lesions are localized; the joints of the limbs and face are mobile; and the disease is of later occurrence. Tetanus neonatorum could develop within eight or nine days after birth if infection occurred upon tying off the cord. It would begin in the face and with greater trismus and other signs of muscular spasm and the temperature curve would be almost the reverse of that of sclerema. Erysipelas neonatorum also may arise within 10 days from an umbilical infection or from a mother with puerperal fever. In this there is a continuous pyrexia and a sharply defined blush with an advancing margin.

Prognosis.—A fatal termination almost invariably results within 5 to 10 days, the exceptions noted being in some of the cases in which the onset was late or in which the skin was affected only to a limited extent, partial or complete recovery having taken place here, the infant being without severe complications and amenable to treatment.

Treatment.—This is largely symptomatic but some form of treatment should be sought to counteract the toxemia. Extract of thymus gland, 1 to 3 or 4 gr. daily, has been suggested. Most favorable hygienic surroundings and maintenance of strength by proper nourishment are necessary. Rectal feeding and the use of a stomach tube by pharynx or nose become necessary. Measures to bring about increase of the body heat are of greatest import, such as incubation, friction with the warm hand, massage with the inunction of warm olive oil or camphorated oil, baths at 90 to 99°F., of 15 to 20 minutes duration, with or without the addition of mustard or aromatic substances. Internally, whiskey or digitalis preparations in proper dosage should be employed to counteract the cardiac weakness.

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(B) CONGENITAL NEW GROWTHS

BY ERWIN PAUL ZEISLER, M.D.

CHICAGO, ILL.

Nevus Vasculosus.—Definition.—Nevus vasculosus or angioma is a congenital vascular new growth of the corium or subcutaneous tissue. Vascular nevi are the most common congenital new growths of the skin encountered in early life. They represent a localized hyperplasia of the blood-vessels of the skin of varying degree. Clinically, they may be considered in three forms according to the depth of the pathologic process: (1) Flat, vascular nevi composed of a superficial capillary plexus, including the cases described as port-wine mark or nevus flammeus; (2) hypertrophic nevi consisting of a vascular network of considerable size, including the cases described as angioma simplex, angioma simplex hyperplasticum of Virchow, and angioma plexiforme of Winiwarter; (3) cavernous vascular nevi or angioma cavernosum, a deep-seated meshwork of communicating vascular spaces.

Symptomatology.—The flat vascular nevus occurs as macules composed of a fine capillary plexus, varying in color from a bright red to a bluish-red, of variable size and shape and usually found on the face, head, neck or arms. The lesions may be punctiform, coin-sized or may cover the entire side of the head or an extremity. There may be one or a few lesions present and rarely, as in Pollitzer's unique case, they are universally disseminated. They may be present at birth, often show increased growth in the first weeks of life, and are usually persistent. The overlying skin is smooth, but may later become thick and elevated, especially when involving the lips and ears. A special clinical type is the so-called port-wine mark (nevus flammeus), which is an irregular, flat, purple patch covering a large area on the face or head, or spreading onto the mucous membrane of the mouth. Smaller satellite spots are often found at the border of the main lesion. Pressure or exposure to cold may obliterate the color momentarily. This type is usually present at birth and is likely to persist throughout life.

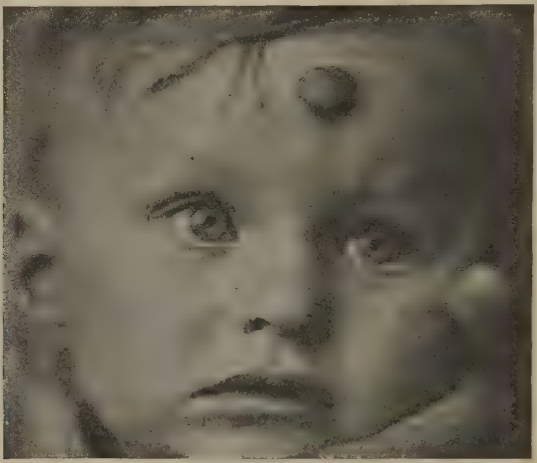

Fig. 4.—Angioma of the forehead.

The hypertrophic nevus is the more common type of angioma (popularly called "strawberry mark"), and appears at birth or several weeks later. It is usually smaller than the flat nevus, varying in size from a pea to a walnut, but may grow rapidly in the first weeks of life until it covers the entire face or side of the head. It is an elevated, soft compressible tumor of purplish color. The surface is smooth, nodular, or may have polypoid protuberances. The lesion is turgescent and may even show distinct pulsation. Crying, coughing, or a dependent position temporarily increase the size and turgescence of the lesion. On the other hand, the color fades and the size diminishes under digital pressure or when the part is elevated. In some types there is a new formation of veins in the subcutaneous tissues, this constituting the venous nevus.

Hypertrophic nevi occur on the head in 75 per cent. of cases. The cheeks, forehead, lips, nose, ears, eyelids and mucous membranes of the mouth are familiar localizations. The upper lip may hang down as a pendulous fold over the lower lip. The ear becomes enormously enlarged and may pulsate. The tongue, when involved, often becomes so large as to interfere with deglutition. Large angiomas of the limbs are occasionally associated with an elephantiasic thickening of the entire limb, consituting the so-called angio-elephantiasis.

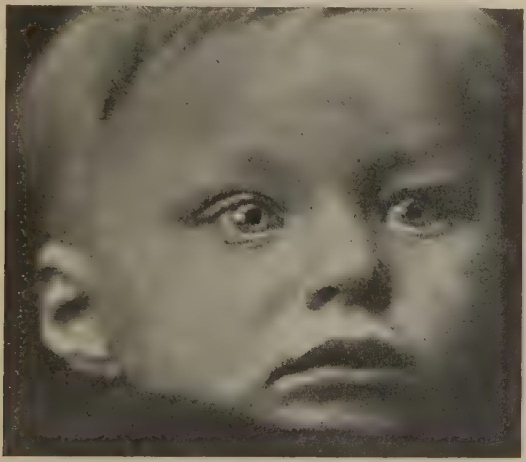

Fig. 5.—Angioma of the forehead after treatment with radium.

Angioma cavernosum is a more deeply seated lobular tumor of deep blue or purple color, with a tendency to persistent destructive growth, which manifests itself soon after birth. The tumor may at first be a small encapsulated growth which remains stationary, or it may be more diffuse and lead to rapid destruction of the neighboring tissues, including cartilage and bone. Subcutaneous cavernomas shine through the overlying skin as bluish nodules. When they communicate with the larger arteries they may show transition stages to the plexiform angiomas or racemose aneurysms.

Course.—The clinical course of the different types of angioma is variable. Usually of small size at birth, they either remain stationary during the period of infancy, or grow slowly or rapidly along with the growth of the rest of the body. Hypertrophic and cavernous nevi are most likely to grow rapidly in the first few weeks of life, while flat nevi spread gradually. Occasionally angiomas undergo a process of spontaneous cicatrization in the first years of life, the vascular tissue being replaced by a white atrophic scar. Growths on the cheeks, lips, tongue, vulva or groin may be injured mechanically. The resulting hemorrhage may be severe in the case of small infants, but is rarely fatal. Frequently the subsequent sloughing and ulceration cures the nevus by replacing it with scar tissue. Less frequent pathologic changes are inflammation, thrombosis, calcification, cyst formation and malignant degeneration.

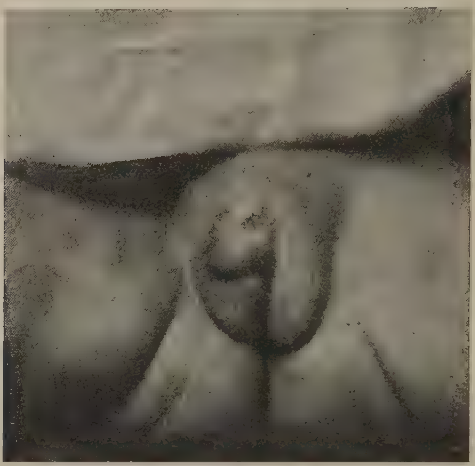

FIG. 6.—Ulcerating angioma of the vulva in an infant.

Etiology.—The etiology of vascular new growths is obscure. Borst and Ribbert emphasize a developmental disturbance on a congenital basis. The peculiar structure, localization, frequent congenital occurrence and the combination with other malformations as encephalocele, spina bifida, cleft-palate or pigmented nevi speaks for a developmental disturbance possibly along the territory supplied by a single artery. A familial predisposition is present in 5 to 15 per cent. of cases. Virchow

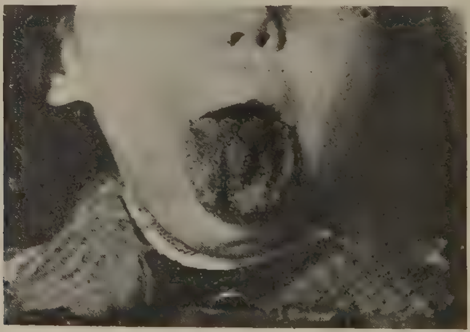

FIG. 7.—Vascular nevus of the tongue in a girl 8 years of age.

advanced the theory of fissural angiomas and differentiated auricular, labial, nasofrontal, palpebral and buccal angiomas. Multiple nevi sometimes show a distribution corresponding to a nerve trunk. Unna's belief that intra-uterine pressure from the pelvis is a factor would explain the frequent finding of nevi in the occipital region. The laity are prone to attach considerable importance to prenatal influences, but there is no scientific foundation for this belief. Heredity is a possible factor. Females are more frequently affected than males. Trauma plays an etiologic rôle in some cases of cavernous nevi developing during the first year of life.

Pathology.—Flat, vascular nevi are composed of a plexus of newly formed capillaries situated in the papillary layer of the corium. In the hypertrophic variety dilated newly formed capillaries lined with endothelium occupy the entire derma and subdermal tissues. The cavernous type consists of a communicating meshwork of vascular channels resembling in structure the corpus cavernosum of the penis. The blood spaces may be either venous or arterial in character. According to Ribbert, they have no connection with the normal blood-vessels of the skin or surrounding tissues.

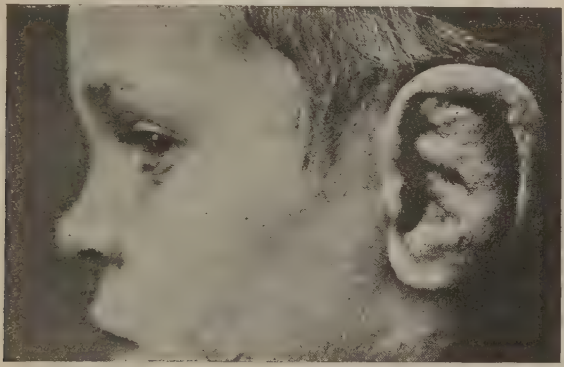

Fig. 8.—Pulsating angioma of the ear in a boy 5 years of age.

Diagnosis.—The diagnosis of an angioma in an infant presents little difficulty. An ulcerated nevus may give rise to difficulty in diagnosis, but the history will often be a guide. Encephalocele is readily differentiated by its location, lobulation and characteristic pulsation.

Prognosis.—The prognosis of angioma in infants must be guarded. It is necessary to watch the rate of growth, destructive tendency and response to treatment before arriving at definite conclusions. Many small nevi undoubtedly disappear spontaneously and should be left alone, particularly if in an inconspicuous location. Port-wine stains are permanent and in extensive cases little can be accomplished by treatment. Much depends on whether the color disappears on pressure.

Treatment.—The indications for the treatment of angiomas are chiefly cosmetic, except when there is a severe hemorrhage or destructive tendency. Unless there is a marked increase in size in the first few months, it is perhaps best to delay interference until the end of the first year. The only absolute contra-indication to treatment in infancy is some severe general disease. As many methods of treatment have been advocated from time to time, it will be advisable to consider these in order. The choice of the proper method will depend entirely on the individual case, with particular consideration of the depth, extent and character of the growth.

1. *Compression Treatment.*—Small nevi in infants can at times be successfully eradicated by daily painting with flexible collodion, as recommended by Unna, or by long-continued pressure with bandages or adhesive straps as Lexer and von Bergman advise, when the growth is located over a bony prominence.

2. *Cauterizing Agents.*—Among the many caustics that have been recommended may be mentioned carbolic acid, fuming nitric acid, zinc chlorid, caustic potash, arsenic pastes and trichloracetic acid. The chief contra-indication to their use is the difficulty of regulating their action and the danger of severe scarring. A concentrated solution of trichloracetic acid is the most suitable. It may be painted on the surface or bored into the growth and neutralized with alcohol or water after a few seconds when the lesion becomes white. The author has had good results in the treatment of superficial nevi with trichloracetic acid.

3. *Injection Treatment.*—Wyeth, Porter, Reder and others in America have obtained good results in subcutaneous cavernomas by injection of boiling water under general anesthesia. Schwalbe recommends the repeated injection of 1 to 3 c.c. of 50 to 75 per cent. alcohol, but this method is not devoid of danger.

Payr introduces sharp spicules of pure magnesium aseptically into cavernous nevi, with marked improvement as a result of the chemical interaction with the tissues and subsequent shrinkage.

4. *Operative Procedures.*—Many operative measures, including multiple scarification, simple incision, ligation, excision and plastic procedures have been advised by surgeons. Excision is justified only in encapsulated angiomas. Compression or ligation of the main arteries of supply rarely gives results. Operative measures should be reserved for large lobulated angiomas.

5. *Heat.*—The Paquelin cautery and Unna's "microbrenner" are occasionally successful. The heat causes necrosis and thrombosis.

6. *Cold.*—Liquid air has been used, but is difficult to obtain and has many technical disadvantages. The most universally suitable method for moderately sized nevi is freezing with carbon dioxid snow, at first used by Pusey and subsequently advised by Zeisler, Bunch, Morton and many others. The snow is easily obtainable, convenient to use and gives good cosmetic results. It can be used on the mucous membranes as well as on the skin. It gives better results in hypertrophic

nevi than in the *nevus flammeus* type. A proper technique is important. The snow is molded into a firm mass corresponding to the size of the lesion, and is applied with firm pressure for from 20 to 60 seconds, depending on the depth of the lesion. The first effect is to freeze the tissue into a white depression which thaws out after a few minutes, and within an hour shows an inflammatory reaction with a blister. The latter should be kept intact if possible and allowed to dry into an adherent scab, which falls off in the course of a week. The process may have to be repeated. The snow has an apparently selective action on vascular tissue, possibly aided by subsequent serotactic action, and seldom leads to keloid formation. It has been the method of choice in the author's hands over other cauterizing, electrical or operative procedures. Sibley suggests that the carbon dioxid snow be dissolved in acetone and applied to the nevus with a camel's hair brush.

7. *Electric Procedures.*—The galvanocautery, high frequency or D'Arsonval current, electrothermic coagulation (Clark) and other similar methods have their advocates. Electrolysis is especially useful in punctiform nevi and telangiectases. A current of from one to four milliamperes is used with the needle attached to the negative electrode, while the other electrode is applied to the palm of the hand with a wet sponge. The needle is introduced at a slant for a distance of ¼ to ½ in. at several points and the current allowed to run for one-half to one and one-half minutes till the color of the lesion is blanched. This method is useful in selected cases, but is rather painful and, therefore, difficult to use in children.

8. *Roentgen-ray.*—The *x*-ray has not hitherto been uniformly successful in the treatment of angiomas. The object is to produce a slight dermatitis which will lead to obliteration of the blood-vessels. The possibility of ulceration, scarring and subsequent telantiectasia and atrophy from over-treatment must be borne in mind.

9. *Radium.*—According to Wickham and Degrais and subsequent workers, the beta rays of radium have a specific effect on vascular endothelium. With proper attention to technique and careful screening, angiomas can be obliterated without producing severe inflammatory reaction or ulceration. Round or square, flat "varnish" applicators containing from 5 to 20 mg. of radium element evenly distributed over the surface are usually employed, or tubes containing 25 to 50 mg. can be used. The author uses a half-strength placque containing 10 mg. of radium element screened with 0.1 mm. silver or aluminum; several layers of black paper and wrapped in thin rubber tissue. This is strapped with adhesive over the area to be treated for a period of four or five hours in divided doses. After an interval of several weeks the exposure is repeated until the desired blanching of the lesion is obtained. When using square applicators it is important to avoid a checker-board effect by frequent change of position, or keeping the radium applicator slowly moving over the surface. In large angiomas tubes are employed most effectively by the cross-fire method, or radium

needles can be buried in the growth. The cosmetic results in the hand of experienced workers are beautiful, but it should not be forgotten that radium, as well as the Roentgen-ray, can cause a subsequent atrophy and telangiectasia as disfiguring as the original condition if improperly used. The ease of application and painlessness are important factors in giving radium first place in the management of birthmarks in childhood.

10. *Phototherapy.*—The Kromayer mercury-vapor lamp has been highly extolled by a number of authors in this country, but does not always give uniform results. It is used under compression, and may cause a severe reaction. It gives fair results in superficial angiomas, and is sometimes combined with radium in the treatment of port-wine marks.

Nevus Pigmentosus. Definition.—A pigmented nevus or mole is a congenital lesion of the skin characterized by circumscribed areas of pigmentation with or without alteration of the other structures of the skin.

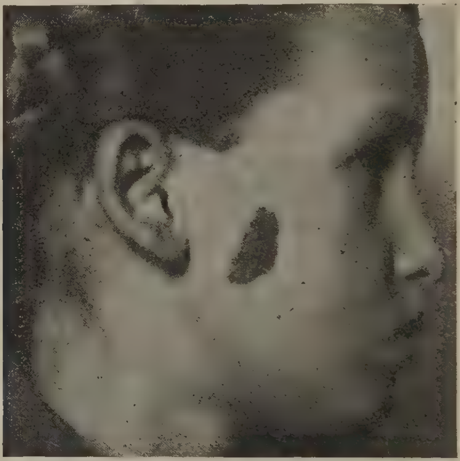

Fig. 9.—Nevus pigmentosus in a girl 10 years of age.

Symptomatology.—Pigmented nevi are usually present at birth but may not appear till a few months or years later. Exceptionally they may appear a long time after birth, but probably in every case an embryonic defect is present which was at first unnoticed. Moles do not increase in size very much, but with the growth of the individual may become more pronounced, rougher or more hairy (Pusey). There is no tendency to spontaneous disappearance. The flat mole or *nevus spilus* is a light or dark-brown pigmented macule, varying in size from a pin-point to an area covering many square inches. Children often present numerous small moles scattered over the body or one or more larger lesions covering extensive areas on the trunk or limbs. There is no special symmetry noticeable, but occasionally the distribution suggests the course of a nerve. The so-called linear nevus is usually considered under the heading of ichthyosis hystrix.

According to the predominance of certain anatomic features, nevi are usually designated by special descriptive terms. *Nevus pilosus* refers to markedly hairy lesions, the mole being covered with a growth of fine or coarse light to dark hair. *Nevus verrucosus* is a rough, warty growth which Unna divides histologically into acanthoid and keratoid, depending on whether there is hyperplasia of the prickle layer or the horny layer. *Nevus papillomatosus* presents papillary excrescences. *Nevus lipomatodes* shows a preponderance of fat and connective tissue and occurs as soft, lobulated or cerebelliform growths. These non-pigmented yellowish moles without hair are occasionally seen in children, but are not as common as the pigmented forms. *Nevus sebaceus* is associated with a hypertrophy of the sebaceous glands of the skin. A special type of nevus is the giant nevus or "bathing trunk" variety, covering the lower lumbar region, the buttocks and the upper part of the thighs. Howard Fox collected some 25 instances of this type. It is usually a yellowish-brown nevus covered with downy hair. It is significant that pigmented nevi in children are often found conjointly with other developmental anomalies as multiple fibromas, vascular nevi, harelip, etc.

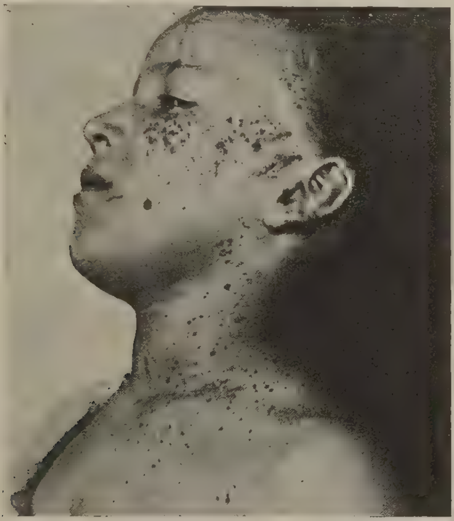

FIG. 10.—Multiple pigmented nevi in a girl 5 years of age.

Pigmented nevi last a life time and in later years may give rise to serious trouble. As a result of irritation, they undergo a peculiar malignant degeneration and the resulting melanotic growths are exceedingly malignant.

Etiology and Pathology.—Most moles are congenital, although Duhring states that certain smooth, non-hairy nevi of the trunk are acquired. Unna believes in the hereditary basis of all nevi.

Pathologically, characteristic parallel rows or masses of cuboidal cells are found in the corium extending down from the basal layer of the epidermis and separated by thin connective tissue septa. A great deal of discussion has taken place regarding the origin of these "nevus" cells. Many pathologists, following Virchow and Kaposi, consider them of connective tissue or endothelial origin. On the other hand, Unna, Hutchinson, Gilchrist and others look upon them as derived from the epidermis. Kromayer thinks the nevus cells are snared-off epidermal cells which have lost their prickles and become converted into connective tissue cells by a process of metaplasia.

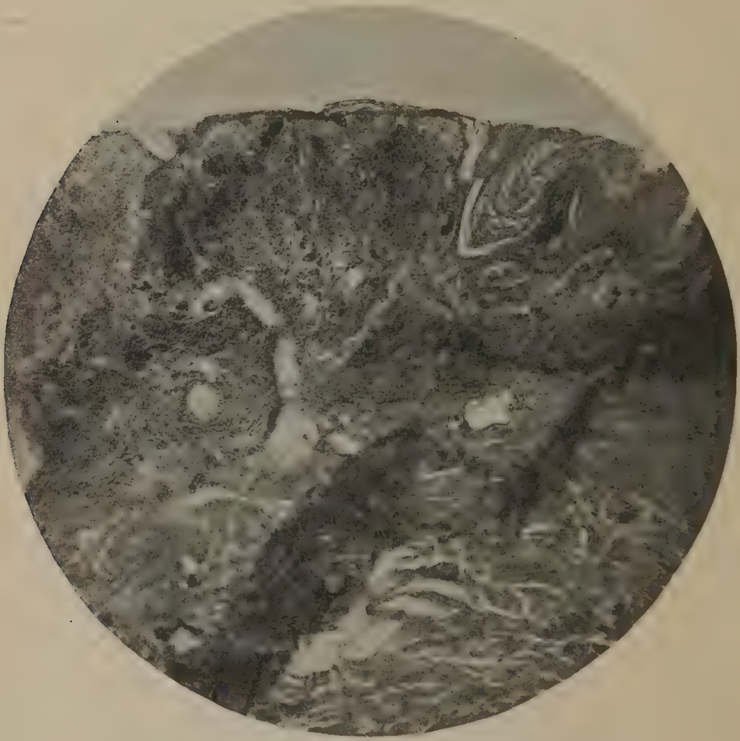

Fig. 11.—Nevus pigmentosus—low magnification.

There is an increased amount of pigment in the lower layers of the epidermis. The pigment in the nevus cells is derived from the malanoblasts which are in contact with the nevus cells. All the cutaneous structures may show more or less hypertrophy, especially the hair-follicles.

Diagnosis.—The diagnosis of pigmented nevi offers no difficulties.

Prognosis.—Pigmentary nevi run a benign course during infancy and childhood and cause no trouble aside from the disfigurement produced. Later in life malignant change may take place.

Treatment.—The chief indication for the treatment of pigmented nevi in childhood is a cosmetic one. Flat pigmented nevi can be successfully treated by repeated application of a saturated solution of trichloracetic acid, or by painting several times with sublimate-salicylic acid collodion. For circumscribed soft nevi, the best treatment is excision. Large nevi can also be excised and the defect covered by skin grafting, but this method is liable to result in hypertrophic scars. Small moles can be removed with electrolysis, allowing the current to pass in various directions. In the case of hairy nevi the destruction of the hairs by the electric needle with additional transfixing of the nevus in several planes parallel to the surface will usually suffice to remove the blemish. In children it is somewhat

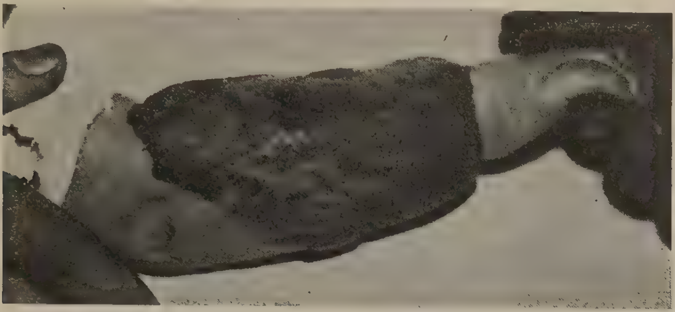

Fig. 12.—Sleeve-like vascular nevus of the forearm in an infant four months of age.

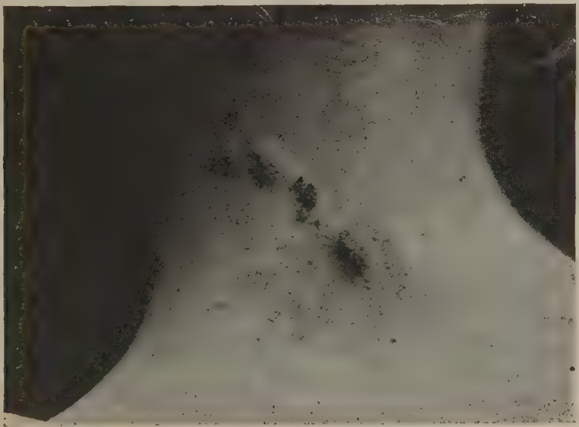

Fig. 13.—Nevus verrucosus.

difficult to use the electric needle and other methods should be given preference. The author has had considerable success in removing even extensive nevi by freezing with carbon dioxid snow. The solid stick is pressed firmly against the lesion for from 30 to 60 seconds. The resulting bulla is permitted to dry, and the hair and pigment come off when the crust falls off. The process may have to be repeated, but will nearly always give a good cosmetic result. Radium has been advocated to remove the hair in small, hairy moles but is slow in its action. Recently the author has found the electro-cautery an exceedingly useful agent in the removal of pigmentary valvi. A flat cautery blade is lightly pressed against the lesion for a few seconds using a low degree of heat. This method does not leave scars. Surgical diathermy may also be used successfully.

Lymphangioma Circumscriptum.—**Definition.**—A rare new growth of the lymphatics of the skin originating in infancy or childhood and consisting of groups of thick-walled vesicles, discharging lymph when punctured. The disease was first described by Tilbury Fox. Various synonyms for the disease are lymphangioma cavernosum (Besnier), lupus lymphaticus (Hutchinson), lymphangiectodes, and lymphangioma capillare varicosum. The various other lymphatic new growths which affect the cheeks, tongue (macroglossia), lips (macrocheilia) or eyelids, as well as the cystic hygromas of the neck properly belong to the domain of surgery.

Symptomatology.—The disease begins in childhood as small groups of opalescent vesicles, deeply seated in the skin. There may be one or more circular or band-like clusters, 1 to 3 in. in diameter, of firm yellow or reddish vesicles varying in size from a pinhead to a small pea. The overlying epidermis becomes thickened and warty and the surrounding area at times assumes an elephantiastic condition in long-standing cases. Telangiectases are present over the roofs of the vesicles and in the adjacent skin. The vesicles are not readily ruptured but when punctured emit a clear colorless lymph, with at times a reddish tinge, but without resulting lymphorrhea. When ruptured the vesicles become covered by thick adherent crusts. The sites of predilection are the upper extremities, the neck, scapular and axillary regions, occasionally the mouth and lips. The author has seen several cases in children shown at the New York and Chicago Dermatological Society Meetings with groups of lesions on the neck. Tobias has recently reported a unique case of lymphangicetatic hypertrophy of the vulva which began at birth and was associated with a nevus unius lateris. Occasionally the vesicles develop at the site of a hemangioma or deep-seated lymphangioma. In a large percentage of the recorded cases the affection has been on the left side of the body. Recurrent inflammatory atacks limited to the affected areas have been observed and have been compared to the "erysipelas" that occurs in elephantiasis.

Etiology.—The exact cause of lymphangioma circumscriptum is unknown, although it is probably of congenital origin, most cases originating at birth, in infancy or childhood. Nevi are often observed in the same patient. Various theories have been advanced to explain the pathogenesis of the disease. Unna assumes the simultaneous occurrence of lymphatic and venous stasis preliminary to the abnormal congenital tendency to proliferation of the endothelium and perithelium. Török and others assume a primary new-formation of lymph vessels with subsequent dilatation. Pollitzer from his studies concludes that a deep-lying obstruction, either lymphatic or conjointly venous and lymphatic, is the first event in the chain that leads to the formation of a lymphangioma.

Pathology.—The histopathology has been investigated by White, Gilchrist, Pollitzer, Brocq and Bernard, and others. The upper part of the corium shows numerous newly formed lymphatic channels in the form of cyst-like spaces. These cavities have an endothelial lining, are subdivided by septa composed of unaltered corium, and are filled with coagulated lymph, leukocytes and occasionally red blood cells. There is a variable amount of small-celled infiltration around the cysts (Bowen). The vascular dots seen macroscopically over the vesicles are caused by dilated capillaries between the epidermis and the

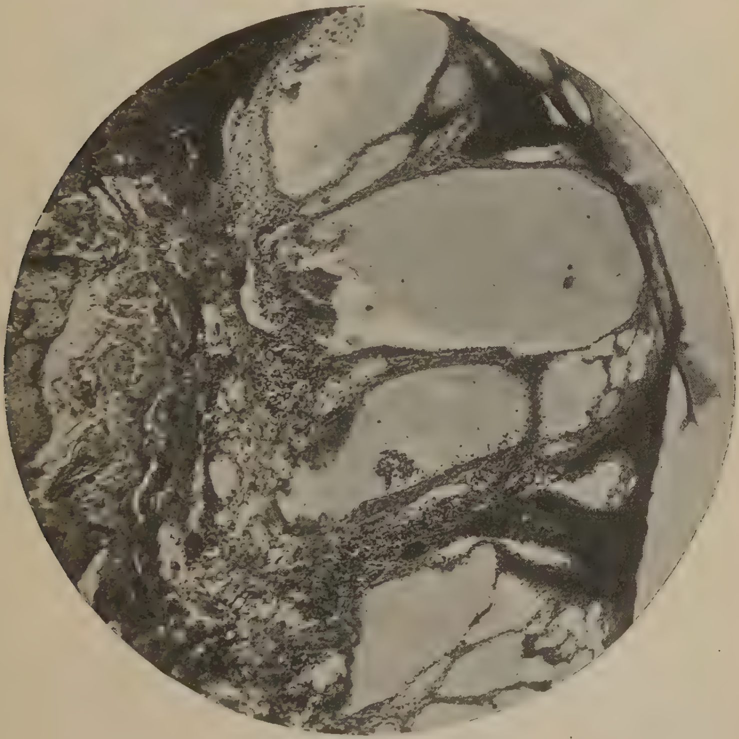

Fig. 14.—Lymphangioma circumscription (low magnification).

upper wall of the cyst-like spaces. In some instances the presence of numerous dilated blood-vessels in the corium has led to the suggestion that these growths are pseudo-lymphangiomata or hemangiomata in which the blood cysts have been filled with serum and converted into clear vesicles.

Diagnosis.—The presence of clusters of thick-walled vesicles, discharging lymph when punctured, associated with telangiectases and having their origin early in life is sufficient to make a diagnosis.

Prognosis.—The disease runs a benign course in the majority of cases and may remain stationary for years. There is no tendency to spontaneous disappearance. Stelwagon has noted a tendency of the patches to shift and recurrences are prone to occur after surgical removal, new vesicles appearing at the borders of the scar.

Treatment.—Excision, electrolysis and curetting have been tried but on account of the danger of recurrence should be supplemented by the use of the *x*-ray. Radium has been successfully used by Simpson in one case. Engman and Mook recommend the *x*-ray.

Adenoma Sebaceum.—**Definition.**—Adenoma sebaceum is a rare disease, probably of congenital origin, characterized by small multiple tumors originating in the sebaceous glands about the nose and adjacent parts of the face. Not over 50 cases are recorded in the literature, the first instance being reported by Rayer. Since Pringle's study in 1890 it is often referred to as Pringle's disease.

Symptomatology.—Minute, discrete, yellowish-red nodules are found in the skin of the face, either at birth, early childhood or rarely at a later age. Ricker and Schwalb note that 15 out of 19 cases began in childhood. The color of the nodules varies from yellow to red depending on the varying amounts of sebum contained, and the presence of telangiectases covering the surface. They are grouped symmetrically about the nose, naso-labial folds and cheeks. Poór has called attention to an asymmetrical variety which may occur on other parts of the body and may coalesce. Growth is slow; the nodules seldom become larger than a split pea, and remain stationary for years. Exceptionally there is more rapid growth at puberty and involution is rare.

Etiology.—The disease is very probably congenital and other defects of the skin are present as warts, nevi, fibromas, lipomas, etc. Many of the cases, especially in England, have been observed among the inmates of asylums, in feeble-minded children, epileptics or imbeciles. A family incidence is occasionally seen. Taylor and Barendt report three cases in one family, and Adamson observed the lesions in mother and child. Fisher and recently Olson report the association of adenoma sebaceum with tuberose brain sclerosis and renal tumors, particularly teratoma. A combination with von Recklinghausen's disease has also been noted.

Pathology.—The tumors have their origin in the sebaceous glands and histologically show large or small masses resembling the hypertrophied acini of sebaceous glands. Sutton's histologic study showed both hypertrophy and true tumor formation. A simultaneous involvement of the sweat glands has also been pointed out by Crocker. Adenomata of the sweat glands (spiradenoma-adenoma sudariparum) are rare occurrences, being found as small tumors on the neck or trunk developing about the age of puberty.

Diagnosis.—The location of the nodules, their congenital origin, benign tendency, and the frequent association with telangiectases and other cutaneous defects, is sufficiently characteristic in most cases for a diagnosis, although it is advisable to confirm this microscopically. In children, particularly, molluscum contagiosum and colloid milium should be ruled out.

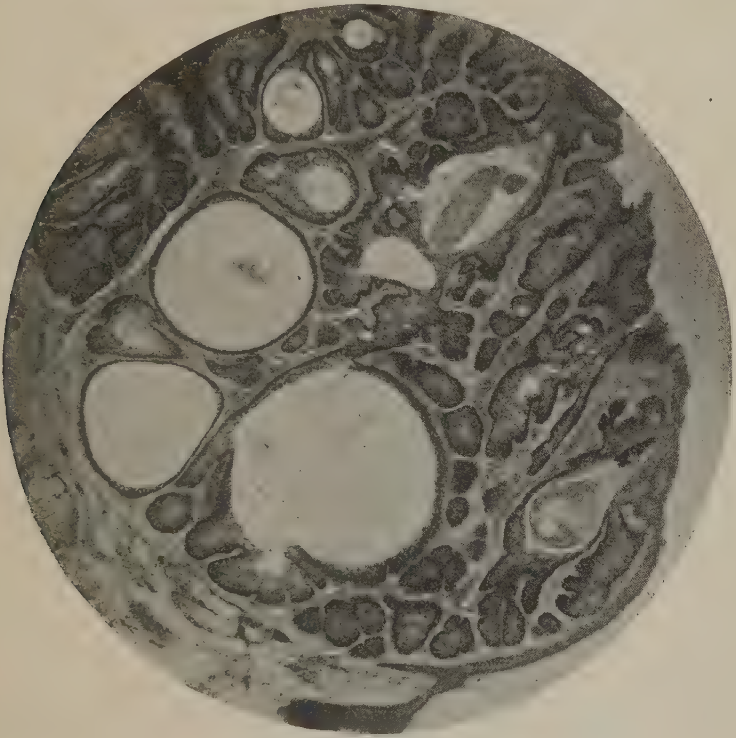

FIG. 15.—Adenoma sebaceum (low magnification).

Treatment.—Excision is the only treatment for the lesions of adenoma sebaceum.

Multiple Benign Cystic Epithelioma.—**Definition.**—Under this title are included two groups of multiple benign cystic epithelial tumors which frequently begin early in life and about whose nature and origin there exists considerable diversity of opinion. The first group includes the cases described as the Brooke-Fordyce type of epithelioma or acanthoma adenoides cysticum, trichoepithelioma, epithelioma adenoides cysticum, etc. The second group includes the sweat-gland tumors designated syringoma or syringocystoma, described by Kaposi in 1876 as lymphangioma tuberosum multiplex, and by Darier in 1887 as hyrodenomes éruptifs.

Symptomatology.—The lesions described as epithelioma adenoides cysticum are solitary or multiple, grouped, symmetrical, pearly nodules with a predilection for the face, especially the nose, eyelids, forehead, cheeks and scalp. Less commonly the nodules are disseminated over the neck and upper extremities. They are firm, pea-sized tumors, of variable color, yellowish or reddish which grow slowly and remain stationary after puberty. Walters has described a congenital case. A distinct family predisposition has been noted by Brooke, Sutton and Fordyce, the majority of the cases occurring in females. A hereditary tendency has been also observed, the disease appearing in several members of two generations. There are no subjective symptoms. Ulceration or malignant change is exceptional, although reported by a few authors.

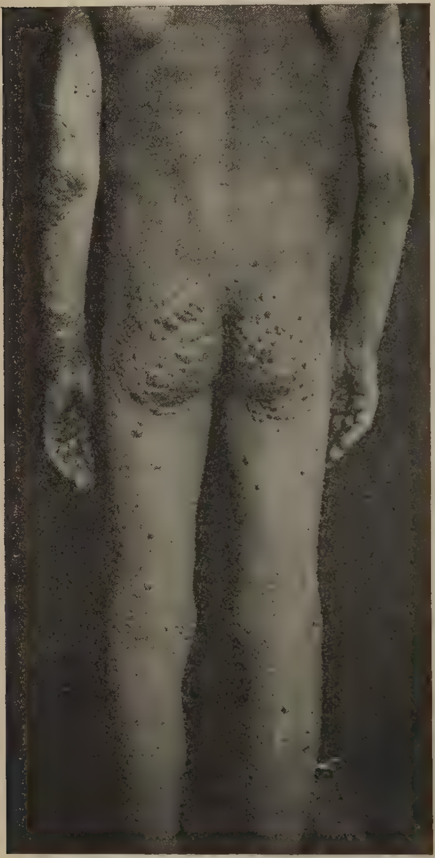
Fig. 16.—Xanthoma tuberosum in a boy 9 years of age.

The lesions of the syringoma group are multiple pinhead to pea-sized, flat or rounded, soft nodules, growing slowly and gradually increasing in number and size. Most of the reported cases have been in adolescent females, but the age of onset is often early in life. In 47 cases, 27 began in the first decade, 5 in the second decade, and 11 in the third. In McDonagh's case the lesions developed at the end of the first year. The favorite sites are the anterior part of the chest, the neck, side of the thorax, and rarely the face and scalp. Occasionally the lesions are scattered over the abdomen, arms and back as in Ormsby's case. The color varies from a yellow to a brownish-red with a very glistening surface. The tumors themselves give no symptoms. A hereditary and family disposition is rare although observed by Elschnig (two sisters and mother), Gassman (daughter and mother), and others.

Etiology and Pathology.—Aside from the onset early in life, the occasional family or hereditary occurrence, and the predisposition to females, little is known regarding the causation of these tumors. The epithelioma adenoides cysticum tumors are derived either from the basal layer of the rete or from the epithelium of the hair follicles. Extending downward into the cutis from the basal layer of the epidermis, Sutton found numerous long, slender chains of epithelium two or three cells in width which terminated in bulb-like cysts, filled with colloid substance and corneous material. The outermost covering of the club-shaped projections consisted of a layer of cylindrical epithelium. The inner zone was composed of imperfectly stained, rounded, epithelial cells, encircling a central zone of debris. There is some question as to the relation of the benign cystic epithelial tumors to the multiple rodent ulcers and transitional cases have been reported by Graham-Little and Adamson.

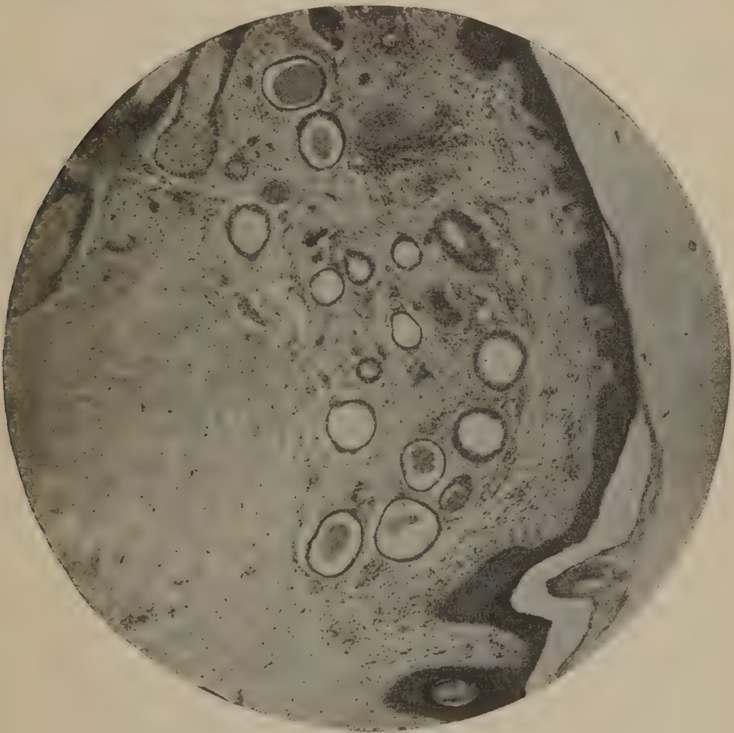

FIG. 17.—Syringoma—low magnification.

The syringoma group of tumors are derived either from normal sweat ducts or congenitally misplaced ducts. The occurrence of the disease in children and in several members of the family favors the congenital theory. An associated disturbance of the sweat secretion has been noted by White. Microscopically there are found in the middle corium scattered branching epithelial buds and cysts of the diameter of sweat ducts. By occluding the sweat ducts similar cysts have been produced. Sutton showed that the cells lining the tubules still retained their function by administering pilocarpin, sweat droplets showing on the surface of the tumors.

Diagnosis.—The diagnostic features of the epithelioma adenoides cysticum group are its onset in childhood or at puberty, its occurrence in several members of one family, and the presence of persisting, pearly, symmetrical nodules on the face and scalp chiefly, occasionally terminating in ulceration or malignant degeneration. The syringoma group is characterized by the presence of numerous soft, slowly growing nodules situated chiefly on the trunk of adolescent females, and showing histologically a more tubular arrangement resembling embryonic sweat ducts. Nevertheless, many authorities contend that the two groups are histologically indistinguishable and classify both under benign cystic epithelioma. In children the lesions of molluscum contagiosm and adenoma sebaceum are especially to be differentiated.

Prognosis and Treatment.—In the majority of the cases the tumors remain stationary after attaining a certain size and malignant change is rare. The lesions may be excised, curetted, frozen with carbon dioxid snow, touched with trichloracetic acid, or radium and the Roentgen-ray may be employed.

Neurofibroma—von Recklinghausen's Disease.—Definition. Von Recklinghausen's disease comprises those cases of single or multiple fibrous tumors of the skin derived from the sheath of a cutaneous nerve, beginning at birth or in early life. The disease was described by Ludwig in 1793 and the name molluscum fibrosum was given to it by Virchow. Since the publication of von Recklinghausen in 1892, pointing out the true nature of these multiple tumors as neurofibromas, several hundred cases have been reported in the literature.

Symptomatology.—The disease usually begins at birth or in early life as one or more small, deeply situated, subcutaneous nodules associated with pigment spots. There is a gradual development of new tumors and increase in size of old ones as the patient grows older. The tumors are characterized by their soft, doughy consistency, transparency and mobility, and are covered by normal skin, which later becomes pigmented or bluish-red. Fully developed tumors vary in size from a pea to a nut, are round or pear-shaped, sessile or pedunculated. In certain cases one or more pedunculated tumors attain an enormous size constituting the type known as fibroma pendulum. These are prone to develop where the skin is loose, as on the face and back. In other cases the tumors numbering hundreds and even thousands are scattered over the entire integument and along the nerve trunks. In one of the author's cases there were thousands of tumors, chiefly on the trunk. After a number of years tumors may cease to form and the disease remain stationary, some of the older tumors even undergoing involution, and leaving bags of wrinkled skin in their place. In some cases the course of the disease is definitely influenced by metabolic changes. Puberty may be the stimulus to generalization of the tumors.

Pigmentations are noted in about one-fourth of the cases either at birth or later in life and are indistinguishable from freckles. They occur as large yellowish-brown placques on the body and may be present long before molluscous tumors have appeared.

Nerve tumors have been observed in about one-third of the cases either as spindle-shaped swellings along the nerve trunks or as plexiform neuromas. The ulnar, radial, orbital, sciatic and crural nerves are most frequently affected. Larger tumors occasionally occur with the formation of elephantine growths, the so-called elephantiasis fibrosum congenita.

Nevi and telangiectases are not infrequently observed in von Recklinghausen's disease and several authors have noted the association with adenoma sebaceum. In addition, various deformities and malformations in the skeletal structures have been described, notably hyperostoses of the skull, spinal deviations and arthritis deformans. The blood findings reveal a mononucleosis and an eosinophilia. Sarcomatous degeneration is said to occur in 10 to 15 per cent. of cases.

The mentality of the affected children frequently suffers. There is a gradual loss of intellectual power (Hebra) and a tendency to become feeble-minded, despondent and shy. Subjective symptoms are either absent or neuralgic in type.

Etiology.—von Recklinghausen's disease is essentially one of early life and usually both the pigmentations and tumors develop before adolescence. According to Hahn, Hallopeau and others, 40 per cent. of the cases are congenital. The disease has been observed in the newborn. Virchow and others have found that a hereditary and family element is present in a certain percentage of cases. Preiser and Davenport have recently advanced the hypothesis that the hereditary factor is the dominant one. They point out a definite law of recurrence of the disease in certain families, only blood relatives being affected, and a tendency to occur without a break in the generation. Either the father or mother is apt to be affected, whether the affected child is a male or female. Special family types have also been described in which the principal tumors occur in similar locations and are of the same types. Pearse observed the disease in mother and son, Trimble in mother and daughter. Meige has recorded eight instances of elephantiasis fibrosum congenita in four generations of one family.

The exact cause is unknown, although various hereditary, mechanical, toxic and infectious theories have been unheld at various times. The principal views on the nature of von Recklinghausen's disease may be summarized as follows: (1) That there is a congenital and hereditary tendency to the proliferation of the fibrous tissue of the neurilemma sheath which becomes manifest at varying times after birth. This is the most generally accepted view. (2) That it is a disease of the nervous system dating from intra-uterine life. (3) That it is a form of giantism or elephantiasis of the connective tissue elements of the peripheral nervous system. (4) That it is a manifestation of disturbed internal secretions. Elliott and Beifeld contend that the disease is correlated with the status thymicolymphaticus. In their case, in a boy of 16, the disease began at the age of 10 with symptoms resembling Hodgkin's disease. In addition to multiple tumors, nevi and pigmentations, there was adenopathy, enlarged spleen, persistent thymus, scanty axillary and pubic hair, cryptorchism and genital hypoplasia. Other cases showing similar symptoms, were collected, mostly from French literature. This explanation would also account for the numerous instances of lethal ending after operations on large molluscous tumors. Neurofibromatosis has also been observed in association with thyroid changes, cretinism, acromegaly, dystrophia-adiposogenitalis, osteomalacia, tetany and later in life with ovarian and menstrual disturbances. Chauffard and Ramond advocate the adrenal theory based on the finding of enlarged adrenals at necropsy and the occasional association with hypernephroma. The pigmentation and asthenia have also been explained as evidence of adrenal insufficiency. Lastly must be mentioned the interesting observation of Brickner of fibroma molluscum tumors developing during pregnancy.

Pathology.—The tendency at present is to regard the majority of cases of multiple fibrous tumors as neurofibromas. The tumors originate in the neurilemma sheath of the subcutaneous nerve trunks, spreading over to the fibrous sheaths of the sweat and sebaceous glands and blood-vessels. Young tumors are composed of a spongy, edematous type of connective tissue, very cellular and vascular. The older and larger tumors show a denser and coarser fibrous structure. The epidermis is unchanged. Hair follicles are pushed aside. Elastic fibers are present in the connective tissue binding the various parts of the tumor. Nerve fibers can be demonstrated in most cases running parallel to the blood-vessels. The nerve fiber may be stretched or flattened, and when in the center of the growth may be destroyed by pressure.

Prognosis.—Aside from the occasional tendency to sarcomatous degeneration, the growths *per se* are not dangerous. The grotesque, unsightly appearance may make the patient moribund at times, although the general health is not seriously affected.

Diagnosis.—The features of von Recklinghausen's disease—the onset early in life, with multiple tumors of the skin and nerves, and pigmentation, present a characteristic picture. Multiple sarcomas are distinguished by their more rapid growth and ulceration. Lipomas, neuromas and soft moles have to be differentiated when the growths are few in number. Hard fibromas or desmoids are solitary or multiple solid tumors which appear at any age and have been observed at birth. They are seldom larger than a pea, and appear as white or pink, slowly growing nodules on the face, scalp and extremities. They occasionally undergo sarcomatous degeneration.

Treatment.—Little can be accomplished in the way of treatment. Improvement has been reported after arsenic, fibrolysin, and from the use of adrenal extract. Other organo-therapeutic remedies are worth a trial. Large tumors may be removed surgically, but multiple small growths are best left alone.

Xanthoma.—Definition.—Xanthoma is a rare skin affection first described by Rayer and characterized by the formation of benign growths of a yellowish color. There are three clinical varieties: (1) Xanthoma planum; also known as xanthoma palpebrarum or xanthelasma; (2) xanthoma tuberosum or xanthoma multiplex; (3) xanthoma diabeticorum. Of these the most important form occurring in childhood is xanthoma tuberosum.

Symptomatology.—*Xanthoma planum or xanthelasma* occurs around the eyelids as the familiar orange-yellow, chamois-leather patches seen almost always in adults. Only exceptionally do these patches appear in early life and then only as a part of a generalized xanthoma tuberosum. Crocker, however, mentions a case of his, a boy of two with a single xanthomatous placque on one eyelid. Pollitzer has shown that the essential process in xanthelasma differs from that of the other forms of xanthoma and is a fatty degeneration of the muscle fibers of the eyelids.

Xanthoma tuberosum or multiplex occurs as multiple disseminated, yellow or orange colored placques, nodules or tumors varying in size from a pin's head to a bean and in certain cases even growing to the size of a hen's egg. Since the original eight cases of juvenile xanthoma reported by the English Xanthoma Committee in 1882, about 50 additional cases have been reported. The original committee's report gave as the characteristics of the juvenile xanthomas, the onset before puberty, the absence of hepatic disease and the freedom from involvement of the eyelids. Since then a number of cases have been reported in which the eyelids were affected at an early age. In three cases the disease was congenital, with tumors present at birth. In the juvenile type as recorded by Arzt, Winfield, Dubreuil, and others, the cutaneous tumors are present in large numbers, are widespread, and more irregular in distribution than in the adult case. They are also characterized by their lighter yellow or reddish color and smaller size. In other cases developing before puberty without icterus the tumors occur in certain areas of predilection, especially the elbows, knees and buttocks, growing to the size of a hen's egg and characterized by a more intensive yellow or brown color. The lesions are firm, elastic and painless. In exceptional cases the disease affects the viscera. In Knowle's and Fisher's case there was tendon-sheath involvement. Cranston-Low reported a remarkable case with xanthomatous lesions in the heart and tendon sheaths. Lehzen and Knauss described a similar case, a girl of 11, with xanthomatous tumors attached to the extensor tendons of the fingers, and the tendo-Achilles. At postmortem examination patches of xanthoma were found on the mitral valve. In other reported cases the mouth, conjunctiva, cornea, thoracic and abdominal viscera and blood-vessels were affected.

The evolution of the xanthoma tuberosum placques is more rapid than that of the eyelid xanthomas. In Winfield's case, a child of four, brownish macules were first observed which developed in six weeks into typical pea-sized, saffron-yellow xanthoma placques. In other cases the evolution is more gradual. The age of onset in the juvenile cases has varied from a few months to a few years. The disease persists for an indefinite period without affecting the general health, except when visceral lesions are present. Involution is rarely observed and the lesions usually become stationary after growing to a variable size. Subjective symptoms are absent.

McDonagh has described under the title "Nevoxantho-endothelioma" some anamalous cases in childhood with yellowish nodules scattered over the face and body. He regards the cases as nevi undergoing fatty changes. Balzer described as *xanthoma elasticum* a rare eruption of flat, yellow nodules in the folds of flexion, which began in early infancy. Microscopically the tumor was composed of large coils of elastic tissue around the follicles. The disease probably is not related to the other xanthoma forms.

Xanthoma diabeticorum is a special variety of xanthoma occurring in obese adults with an associated glycosuria. The eruption is of more sudden development, consists of discrete papules or nodules, with yellow summits and reddish bases, and is located chiefly on the buttocks, forearms, elbows, knees and back. There is more or less itching and the eruption tends to disappear spontaneously in the course of a few months or years. The youngest case on record is Pollitzer's, a boy of 17. Pusey has described an anomalous case in a boy of 14 who had exanthoma multiplex with diabetes insipidus. Many authorities consider xanthoma diabeticorum as a disease sui generis, while others look upon it as a variety of xanthoma multiplex. The histologic changes are similar but show more evidence of inflammatory action with less connective tissue hyperplasia. The xanthoma giant cells are thought to be fused endothelial cells which have undergone fatty degeneration.

Etiology.—Outside of the possible influence of heredity and a congenital predisposition, little is known of the etiology of xanthoma. In most cases a hypercholesterinemia can be demonstrated in the blood. In many instances it is a family disease and has developed in several generations (Török). Mackenzie, Hyde, Köbner, Hutchinson and Thibièrge have described cases in which several members of one family were affected. In four-fifths of the adult cases there is an associated hepatic disease with icterus occurring prior to or in the course of the disease. This icterus has been interpreted as due to the xanthomatous changes in the liver and bile passages. In most of the juvenile cases which are histologically identical with the adult cases, neither icterus nor glycosuria is present. On the other hand Bazin, Carry-Lepiné, and Török have reported xanthomas developing before puberty which were accompanied by icterus or hepatic disease and were analogous to the adult cases. There may, also, be a diffuse yellowish discoloration of the skin which has been termed xanthochromia without the presence of bile in the urine.

Pathology.—Xanthoma multiplex represents a benign connective tissue neoplasm in the corium. Lying among the connective tissue bundles are large oval or polygonal cells containing one or more nuclei. These are the so-called "xanthoma cells" in which fat droplets and granules can be demonstrated by staining with Sudan III. The fatty material in the xanthoma cells has been shown to be not an ordinary fat but a cholesterol-fatty-acidester, a substance which has also been found in the blood in cases of jaundice and diabetes. The presumption is that the lipoids present in excess in the blood in xanthoma patients pass out through the capillaries of the skin at points of diminished resistance. Chiefly around the joints. Lebedew has produced xanthoma experimentally in rabbits by feeding them cholesterin. Lesions developed only where the skin was traumatized.

Pollitzer and Wile, who have made a special study of the disease, summarize the pathogenesis as follows: "Xanthoma tuberosum represents an irritative connective tissue hyperplasia in which the extravasation of cholesterol-fatty-acid-ester present in excess in the blood acts as the stimulus. The first changes appear in the adventitial connective tissue cells of the smallest blood-vessels of the papillary and subpapillary layers which take up the lipoids poured out from the vessels, proliferate and increase in size, ultimately forming the typical xanthoma cells. The presence of the lipoids in the cells does not appear to affect their vitality except in older tumors where the layers adjacent to a vessel may become completely obliterated by the lipoidal infiltration. The proliferation of the perivascular cells acts in turn as a stimulus to the development of connective tissue which, as fibroblasts and collagenous bundles, surrounds the rest of the xanthoma cells and ultimately predominates over the true xanthomatous elements."

Diagnosis.—The juvenile cases have to be differentiated chiefly from the nodular variety of urticaria pigmentosa. The presence of wheals in the latter disease, the itching, and the characteristic histologic picture showing large numbers of mast cells in the corium are the diagnostic features. Pollitzer mentions a case of multiple dermoid cysts which simulated xanthoma.

Prognosis.—Xanthoma lesions usually persist throughout life.

Treatment.—Large xanthoma lesions must be treated surgically. Smaller growths may be eradicated with trichloracetic acid or carbon dioxid snow. Besnier advises phosphorus in cod-liver oil. Possibly the progress of the disease can be arrested by exclusion of fats from the diet. The diabetic variety in adults disappears under anti-diabetic therapy.

Dermoid Cysts.—Symptomatology.—Dermoid cysts are smooth, globular, doughy swellings either unilocular or multilocular, situated in the subcutaneous tissue. The skin is freely movable over the cyst but the base is often firmly attached to the periosteum of the bone. They vary in size up to a walnut. The outer surface consists of connective tissue while the inner wall has the structure of skin. The contents consist of a yellowish, fatty or cheesy substance, the secretion of the sebaceous and sweat-glands, mixed with epithelial dèbris, cholesterin crystals and numerous hairs, also at times containing teeth, bone and cartilage. Rarely the contents are serous or hemorrhagic. Fistulas with protruding hairs may form.

The localization of dermoids is characteristic. On the scalp they are found in the lines of junction of the cranial bones and may project into the cranial cavity through a depression in the bone. They are common at the root of the nose, in the orbit, at the angles of the eye, on the temples and in the mastoid region. In the mouth they are found projecting under the tongue in the median line, originating in the mesobranchial fold. Dermoids occur in the neck in the region of the second branchial cleft, in the mid-line either above or below the larynx, and also may be found on the umbilicus, genitalia, and in the coccygeal region. Internally, dermoids occur in the various body cavities, testicles, ovaries and other familiar locations.

Etiology.—True dermoid cysts are developmental defects which are formed by invagination of the ectoderm in embryonic life and occur especially at points where there were folds, recesses, or fissures. They may be unnoticed at birth but are often seen during infancy and show increased growth about the time of puberty. They therefore represent true congenital new-growths.

Pathology.—The lining wall of a dermoid has the same structure as skin, with epidermis, papillæ, sebaceous and sweat-glands, and hair. More rarely cartilage and bone is present. In extremely rare cases a dermoid in later life has developed into a carcinoma.

Diagnosis.—Dermoids must be differentiated chiefly from sebaceous cysts, meningocele, lipoma, and other tumors. Sebaceous cysts are rare in early life, are attached to the skin, but freely movable over the bone and are not located over the fetal clefts. Meningocele is more common in the occipital region, disappears on pressure and is frequently of much larger size. It often terminates fatally at an early age. Solid tumors such as lipoma, sarcoma, etc., can be differentiated by aspiration. Dermoid cysts in the neck may be mistaken for thyroglossal or branchial cysts or tuberculous glands.

Prognosis and Treatment.—Superficial dermoids are painless and are not dangerous. Their removal is chiefly for cosmetic purposes. Complete extirpation of the entire cyst is necessary as recurrence will take place if portions of the cyst wall remain in place.

Leiomyoma Cutis.—**Definition.**—This is a rare disease of the skin characterized by pea sized nodules that are usually sensitive and painful.

Symptoms.—The nodules are millet seed to pea sized, round or ovoid, dull red or some shade of brown, moderately elevated and firm to the touch. Early they are insensitive but later become painful. Changes in temperature and cold seasons affect the subjective symptoms. The lesions occur on the extremities, face or trunk. They may be few (two or three) or numerous (a hundred or more).

Etiology.—The lesions may begin as early as the third year. Most cases have been observed in young adults. Nothing is known positively as to the cause.

Pathology.—The nodules are composed of nonstreated muscle fibers running in various directions. The origin has been traced both to the arrectores pilorum and the muscularis of the vessels. In old nodules the fibers are compact which may account for the pain through pressure.

Diagnosis.—The disorder may be mistaken for syringocystoma. From this disorder it is distinguished by the greater elevation of the nodules above the cutaneous surface, their firm consistency and frequent painful character.

Prognosis.—The lesions persist indefinitely unless treated.

Treatment.—Removal by means of surgical excision may be practiced when the lesions are few in number. Electrolysis and freezing with carbon dioxide snow have been used successfully.

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CLASS II. INFECTIOUS DISEASES OF THE SKIN

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(A) Diseases Caused by Cocci

Impetigo.—Synonyms.—German: Eiterflechte; French: Impetigo, Darte humide.

Definition.—Impetigo is an acute contagious disease characterized by vesicles, bullæ, and crusts and is of common occurrence in infancy and childhood.

Symptoms.—The early lesion is a small erythematous spot upon which a vesicle soon develops. The vesicle enlarges, its contents become purulent, which later drys and forms a superficial crust. After several days the crust falls, leaving an erythematous area which gradually fades. The lesions are commonly few in number but may be extensively distributed. The face and hands are the usual sites, although the scalp, forearms, legs and trunk may be involved. The lesions are usually the size of a split pea, but may be smaller or much larger. The base of the lesion is round and its top flat and the crust is so superficial that it has been described as having a stuck-on appearance. The subjective symptoms are mild and though the lesions are often picked, they are not scratched. Occasionally the vesicles enlarge peripherally, clearing in the center, producing a circinate outline (impetigo circinata). In certain epidemics, also in warm climates and in warm weather in temperate climates, and in infants, a bullous type occurs. In these cases the lesions are much more extensively distributed and have rapidly forming bullous lesions which closely resemble those seen in pemphigus. The disorder formerly described as *pemphigus neonatorum* is bullous impetigo and differs from the ordinary cases simply in degree. The vesicles and bullæ are usually situated on an inflammatory base and the contents may be serous or purulent. The bullæ frequently rupture early, leaving a denuded surface which enlarges peripherally. The discharge from these may be scanty or profuse and of a yellowish tinge. In extensive cases constitutional symptoms (elevation of temperature, inappetence, diarrhea and exhaustion) supervene and a fatal termination is the result.

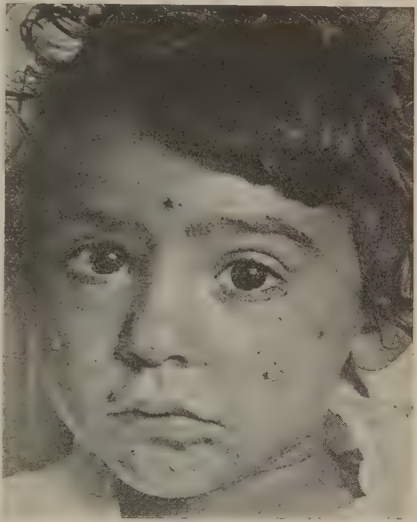

Fig. 18.—Impetigo contagiosa. (Ormsby and Mitchell.)

Etiology.—Impetigo is essentially a pus infection and produced by streptococci or staphylococci or both. Poor hygienic surroundings and filth predospose. Impetigo often is initiated through scratching about the nose and lips by children, the subject of pediculosis capitis. It may follow a pus-infected vaccination or varicella. The disease is commonly transferred directly or through mediate objects from one child to another. The bullous form in infants will frequently spread through a maternity ward, or occasionally a small series of cases occurs in the practice of a midwife. Flies may carry the infection from one person to another. While the disease is common to poverty, it occurs in all grades of society.

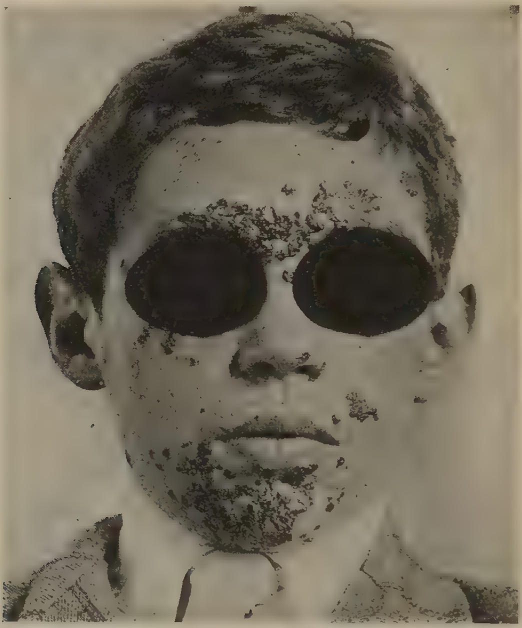

FIG. 19.—Impetigo contagiosa. (Fordyce and MacKee.)

Pathology.—The vesicle is superficially situated, lying between the stratum corneum and rete. Occasionally a streptococcus is obtained in pure culture, but more often either a mixed culture or *Staphylococcus pyogenous aureus* is found. Other varieties of staphylococci have been isolated.

Diagnosis.—Impetigo is to be differentiated from ringworm, pustular eczema and varicella. Ringworm of the glabrous skin occurs more frequently on the trunk and extremities, is characterized by vesicular lesions which spread peripherally and clear in the center and are accompanied by itching. Circinate impetigo spreads peripherally but consists of a single large bulla which dries and heals in the center and is not accompanied by itching and occurs chiefly on the face and hands. In eczema there will be patches with poor definition and some infiltration with irregular crusting, accompanied by itching and weeping. The discrete vesicles generally distributed over the trunk with some constitutional symptoms readily differentiate varicella from impetigo.

Prognosis.—When recognized and properly treated impetigo readily yields, leaving no sequels. In the epidemic bullous type in infants, a small proportion succumb to the disease.

Treatment.—In the ordinary cases the lesions may be bathed with a saturated solution of boric acid. Purulent contents of the lesions are evacuated, an ointment containing 1 to 3 per cent. of ammoniated mercury may be applied at night and a dusting powder containing 1 gm. of mild chlorid of hydrargyrum, 4 gm. of boric acid with sufficient talcum powder to make 30 gm. applied during the day. In older children a solution (1:4000) of mercuric chlorid may be used in place of boric acid. For the bullous cases in infants (so-called pemphigus neonatorum) Foerster[2] obtained good results by applying a 2 per cent. ammoniated mercury ointment on individual lesions after evacuating their contents. A dressing was applied to prevent auto-inoculation. In addition a general bath was given in a warm solution of potassium permanganate. In some cases external heat is applied and strychnia and brand are recommended as supporting measures.

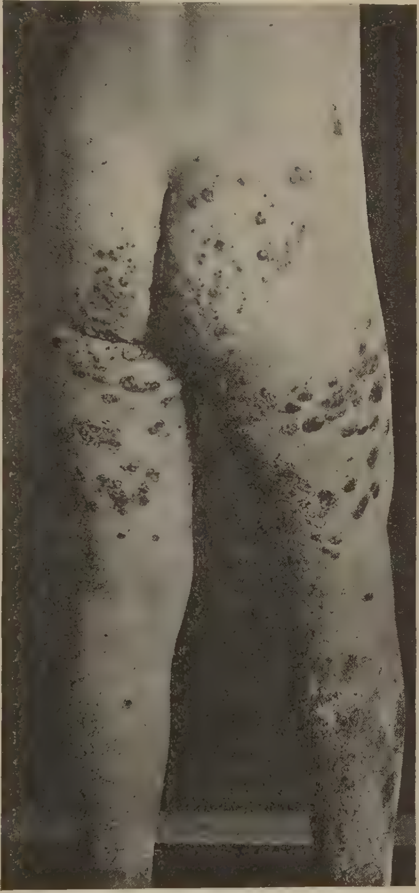

Fig. 20.—Impetigo bullosa. (Fordyce and MacKee.)

Ecthyma.—**Synonyms.**—German: Ekthyma, Eiterblase.

Definition.—Ecthyma is a pustular affection of the skin characterized by heavy crusts and superficial ulceration, occurring chiefly in cachetic children.

Symptoms.—The disease resembles impetigo but is more deeply situated in the skin. The lesions in children are found chiefly about the buttocks and below the knees. The early lesion is a vesicopustule or pustule situated upon an inflamed base. By peripheral extension dime-sized flat pustules are formed which soon dessicate, forming heavy dark-colored crusts beneath which superficial ulceration occurs. In the course of about two weeks the crusts are exfoliated, leaving either hyperpigmented areas or superficial scars. Subjective symptoms are not marked, though there may be some pain and burning sensations present. The lesions may be few or numerous, and the course of the disease varies. As the lesions are auto-inocuable a protracted course may result in a subject of low resistance. Rarely gangrene or lymphangitis may occur as complications.

Etiology.—The disease is commonly seen in public practice in children whose resistance has become lowered by poor food and bad hygienic surroundings or previous disease. The direct cause is a pyogenic microörganism or a group of such microörganisms. Investigators are not in agreement in their findings, some believing the disease is due primarily to a streptococcus and others that a staphlococcus is the causative factor. A greater number of microörganisms are found here than in impetigo. That the two diseases are identical etiologically is demonstrated in patients exhibiting at the same time lesions of impetigo on the face with those of ecthyma on the legs.

Pathology.—The inflammatory process in the corium is characterized by vascular dilatation and perivascular cellular infiltration and marked edema, especially at the periphery. Leukocytes migrate upward into the epidermis. In the severe cases the papillary layer is destroyed, upon the degree of which depends the subsequent scarring.

Diagnosis.—Ecthyma is readily distinguished from impetigo by location and depth of the lesions. Ecthymaform lesions occurring in variola have to be recognized. The pustular syphiloderm is distinguished by its rupioid crust, the greater depth of the ulcer, its induration and the presence of other symptoms of syphilis. The central core, difference in size and shape of the pustule and greater pain differentiates furuncle.

Prognosis.—Recovery takes place in time under proper treatment, but sequels, exhibited as superficial scars and pigmentation, remain.

Treatment.—General care is indicated. Under hospital treatment these patients rapidly recover. Nourishing food, proper hygienic surroundings and tonics, including iron, quinin and strychnia are all indicated.

Local Treatment.—The skin should be cleansed with soap and water, the crusts removed with oily or fatty applications and the ulcers dressed with ammoniated mercury ointment in the strength of 2 to 4 per cent., depending upon the age of the patient. Moist dressings of boric acid or aluminum acetate applied some hours each day are of value. For the salve above mentioned may be substituted a 10 per cent. boric acid or a 2 per cent. mercurous chlorid ointment.

Dermatitis Vegetans.—Dermatitis vegetans occurs in infancy and childhood as well as in adults. Adult cases are recorded in American literature by Hartzell, Pusey, Fordyce and Gottheil, and others. The first report of the disease in infants was made by Perrin. American cases have been recorded by Corlett, and by Wende and DeGroat.

Definition.—The disease is characterized by papillary vegetations occurring in variously sized plaques situated chiefly on the face, but found also at times on the scalp, wrists, arms and legs.

Symptoms.—The primary lesion is a papulo-pustule which either dries and forms a crust or ruptures and discharges its contents, and upon the reddened base the vegetations develop. The plaques are formed either by the growth springing from a single pustule or the coalescence of several pustules. After a short time the lesion becomes crusted and beneath the crust may be seen miliary pustules especially at the border. The fully formed plaque is flat topped and varies in size from a split pea to a walnut and larger, and is elevated from 1/4 to 1 inch above the cutaneous surface. At the periphery new pustules may form. There are no subjective symptoms and no constitutional reaction. The lesions have occurred as a complication in eczema and independently. No sequels follow as a rule.

Etiology.—Wende and De Groat found only staphylococci in the lesions and while positive proof that these were causative is not at hand the evidence obtained suggests this as the probable cause.

Pathology.—In a histologic study made by these investigators, the following findings were made. There was marked hyperplasia of the epidermis, with variously sized and shaped down-growths of the epithelium and marked edema. Mitotic figures were numerous in the prickle-cell layer. There occurred grouping of leukocytes and eosinophils in vesicle-like formation extending to the surface; hyperkeratosis was evident in places while in others the superficial epithelium was lost and replaced by crusts. The corium presented a marked cellular infiltration consisting of leukocytes, polymorphonuclears and lymphocytes, eosinophils, mast and plasma cells. There was marked vascular dilatation and in places the vessels were clogged and the vessel walls showed active proliferation. No microörganism was found other than staphylococcus pyogenes aureus. Cultures made showed the same microörganism in pure culture. Blood examination revealed 2 per cent. eosinophils: Otherwise the findings were normal.

Diagnosis.—The disease is to be distinguished from the eruption due to injestion of bromids or iodids. In the recorded cases positive proof was obtained that these drugs had not been administered. The mildness of the disorder and lack of other signs readily excludes pemphigus vegetans.

Prognosis.—The cases all respond well and quickly to mild local antiseptic treatment.

Treatment.—Boric acid fomentations followed by the application of a mild ammoniated mercury ointment cause a rapid disappearance of the lesions.

Dermatitis Exfoliativa Neonatorum.—**Synonyms.**—Ritter's Disease. Keratolysis Neonatorum. This disease was first described by Ritter von Rittershain who observed 297 cases in a period of 10 years.

Symptoms.—The disease occurs in infants and begins from the second to the fifth week of life. Patches of redness first appear on the face, usually the lower portion, and from here spread rapidly downward over the neck and trunk invading the extremities last. Scaling begins soon in the areas first involved, and rapidly becomes generalized. The scales may be fine and branny, or large and flaky. Coincident with the erythema, vesicles and flaccid bullæ appear, and in these areas crusting occurs. A characteristic feature in most cases is the presence of fissures about the angles of the mouth and other muco-cutaneous orifices. In many cases the areas under the bullæ present a surface resembling that produced by a burn. In uncomplicated cases there are no constitutional disturbances.

The disease runs its course in a week to 10 days, and subsides by gradual lessening of the inflammatory symptoms and return to the normal. Mild recurrences may happen. In other cases the disease persists for 4 or 5 weeks, and is accompanied by gastro-intestinal disturbances and marasmus. Furuncles and abscesses are common sequels. Gangrene rarely follows. Pneumonia may intervene inducing a fatal termination.

Etiology.—The disease as observed by Ritter was seen chiefly in foundlings. He considered it pyemic in nature and non-contagious. Caspary viewed the process as non-inflammatory owing to its afebrile character. Skinner partially confirmed this view in his thorough histologic study of a case in which there was complete absence of the usual leukocytic infiltration that characterizes inflammatory processes. Most observers now agree that the disease is an infection induced by staphlococci and probably a varient of or identical with pemphigus neonatorum. This view was strongly emphasized by Hedinger in his study of two cases. Hazen considers it an infection. He obtained S. albus in pure culture from vesicles in his case. Hoffman found staphlococci as the causative factor and his case presented at different periods symptoms of Ritter's disease and pemphigus neonatorum.

Pathology.—The histopathology as recorded by most observers is that seen in other forms of dermatitis exfoliativa with the added changes due to bullous formation. The case of Skinner above noted is an exception.

Diagnosis.—The disease is only to be differentiated from pemphigus neonatorum and a general exfoliative dermatitis which is occasionally caused by syphilis. As pemphigus neonatorum is now recognized to be bullous impetigo and as Ritter's disease is probably a variety of this disorder, no differentiation is necessary. In the general exfoliative dermatitis due to syphilis, which is rare, other signs of syphilis can be found.

Prognosis.—In Ritter's large series, 50 per cent. succumbed to the disease or its complications.

Treatment.—The nutrition is to be maintained by proper feeding and the body heat is to be conserved by proper clothing. A borated olive oil and lime-water dressing or an oily cream consisting of bismuth subnitrate 4 gm., zinc oxid 8 gm., olive oil and liquor calcis each 120 gm., or a soft ointment, may be applied.

Dermatitis Gangrenosa Infantum.—Synonyms.—Varicella gangrenosa. Pemphigus gangrenosa. Rupia escharotica. Gangrenous infantile ecthyma. Ecthyma terebrant de l'enfance.

Definition.—Dermatitis gangrenosa infantum is characterized by ulcers of varying size and depth occurring in infants and young children, usually following an attack of varicella, though other disorders may precede.

Symptoms.—The early lesion may be a vesicle, vesico-pustule or bulla surrounded by a red areola. The lesion rapidly enlarges and develops a dark-colored slough which is thrown off leaving an ulcer. The ulcers are deep or superficial, round, oval or irregular, vary in size up to an inch or more in diameter and may be ¾ in. in depth. By coalescence large irregular ulcerated areas are at times produced, especially about the lower part of the body, the buttocks and thighs. Other parts affected are the head, face, upper parts of the body and the extremities. The resultant scars depend for their size and other characteristics upon the preceding ulceration. Abscesses occur as a complication and in grave cases marked elevation of temperature, diarrhea and convulsions may supervene.

Etiology.—The disorder occurs as a rule in infants and young children under three years of age. The female sex is most often affected. In children's hospitals an epidemic may follow varicella. Variola, purpura or vaccinia may precede the disorder and it has occurred in infants the subject of tuberculosis, rickets and syphilis. It also occurs independent of these diseases. It is directly due to pyogenic cocci in a susceptable subject. In a case studied by the author, pure cultures of *Staphylococcus aureus* were obtained from unruptured bullæ before death and the same microörganism from the heart's blood post-morten by Dr. Le Count.

Diagnosis.—Gangrenous ulcers occurring in an infant the subject of varicella or other of the exanthematous diseases present a characteristic picture.

Prognosis.—This may be grave when the lesions are extensive or the preceding or accompanying general disorder has reduced the vitality of the patient. Death may result from pyemia on intercurrent lung disorders.

Treatment.—General supportive measures are indicated. Locally mildly antiseptic dressings such as boric acid fomentations, or wet applications of aluminum acetate may be employed. Baths containing mercuric chlorid 1:5000 may be employed with caution. Crocker advises injections of two or three drops of a 2 to 3 per cent. solution of phenol in several places about the ulcers.

Erysipelas.—For discussion see volume VI, page 265.

Erysipeloid.*—Synonyms.—Erythema serpens. Erythema migrans. Crab cellulitis.

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* The disease is described here with reservations as no specific cause has been demonstrated. It appears to be infectious and resembles the streptococcal erysipelas.

Definition.—A mild inflammatory disorder usually occurring on the extremities somewhat resembling erysipelas but unaccompanied by constitutional symptoms.

Symptoms.—The disease occurs, as a rule, on the fingers and hands and is characterized by a patch or several patches of peripherally spreading erythema. The infectious or toxic agent gains access through a wound and the disorder spreads from this point. The abvancing margin of the patch is most active and is well defined and circular or scalloped in outline. As the patch enlarges peripherally, the center undergoes resolution. The patch is bluish-red and slightly edematous. New points begin in the vicinity and undergo the same process of development and involution. Scaling is said not to occur. Slight itching and burning sensations are present but no constitutional symptoms have been observed. The disorder ends spontaneously in the course of a few weeks.

Etiology and Pathology.—The disease occurs in scullions, meat dressers, poultry cleaners, fish dealers and persons of like occupations. In 323 of 329 cases described by Gilchrist,[12] the disorder followed crab bites. The disorder occurs at all ages. The youngest in Gilchrist's series was 17 months. Rosenbach isolated a microörganism of the order Cladothrix, with pure cultures of which he reproduced the disease. Gilchrist and others have been unable to demonstrate any microörganism. Gilchrist believes the disease may be due to a ferment inoculated by the crab. Most observers agree that the disease is probably an infection, the infective agent occurring in decomposing animal matter. Gilchrist found in sections an acute inflammatory process involving the corium and upper portion of the subcutaneous tissue. There occurred a small lymphoid cellular infiltration about the blood-vessels with numerous polynuclear leukocytes throughout the corium. The sweat apparatus was particularly involved. The epidermis was edematous and contained polynuclear leukocytes.

Diagnosis.—Erysipelas, eczema and dermatitis repens are to be differentiated. The mild character of the local inflammatory process together with the absence of constitutional symptoms rule out the first. Eczema is more actively inflammatory and accompanied by marked itching with vesicle formation. Dermatitis repens is a chronic disorder characterized by patches having a raised vesicular margin.

Prognosis.—The disease runs a short course terminating in spontaneous recovery in a few weeks.

Treatment.—Mild solutions of formalin, ichthyol, resorcin or potassium permanganate are efficient; also the mercurials in solution or ointment form. Gilchrist used a 25 per cent. salicylic acid plaster with marked success. The author has had similar results with a 2 to 5 per cent. suspension of chrysarobin.

Multiple Abscesses of the Skin of Infants.—**Definition.**—This disorder is characterized by the formation of variously sized, deep and superficial nodular and tumor-like swellings, irregularly distributed over the cutaneous surface.

Symptoms.—The lesions begin in the skin or subcutaneous tissue, slowly enlarge, soften, rupture and discharge their purulent contents, and heal leaving a scar. They may be red or uncolored and vary in size from a pea to a pigeon's egg or larger, and are practically painless. Some deeper ones may be detected by palpation before they become visible. In feeble infants, ulcers or fistulæ may remain for some time. Folliculitis, lymphangitis and suppurative adenitis may occur as complications.

Etiology.—The disorder occurs in feeble infants whose health has been reduced by poor food, bad hygienic surroundings and disease. Neglect in the early stages induces marked increase in the smaller lesions due to auto-inoculation. The direct cause is *Staphylococcus pyogenes*. The mode of infection has been the subject of much study and it is now the generally accepted view that the disorder is a local infection spread by auto-inoculation.

Diagnosis.—Gummata of syphilis and cold abscesses of tuberculosis must be differentiated. The former is rare in infants and the course of the lesions differs and other manifestations of syphilis may be found. The cold abscess too may be associated with tuberculosis of other parts of the body.

Prognosis.—In mild cases recovery soon follows proper treatment. In others the result depends upon the attendant disease and complications.

Treatment.—The general condition is to be improved by proper food and general care. The abscesses are to be opened, drained and dressed with moist antiseptic compresses. General baths with boric acid or permanganate of potassium are recommended to prevent auto-inoculation. Autogenous vaccines may be employed.

Furunculus.—**Synonyms.**—Furuncle. Boil.

Definition.—A furuncle is a localized infection of the skin characterized by tenderness and pain and terminating in suppuration and necrosis.

Symptoms.—Furuncles occur frequently in children particularly in the warm season and in infants often in association with multiple abscesses. The early lesion may be a small pustule, frequently at the site of a hair follicle. The are a around the pustule becomes red, swollen, tender and painful and in the course of a few days the lesion ruptures and discharges its contents. At other times the early lesion is a smaller, comparatively deeply situated nodule which enlarges rapidly, becomes red, tender and painful and shows, after a few days, a yellow point in the center indicating suppuration in the deeper tissues. Upon rupture in either case pus admixed with blood is discharged, together with necrosed tissue, the so-called "core." When this occurs, the subjective symptoms are relieved and the lesion heals rapidly by granulation leaving a reddened area which gradually disappears and a permanent scar which varies in extent depending upon the amount of necrosis which preceded. The lesions are usually from pea to nut sized and may be single or multiple or develop in successive crops. The scalp, neck and buttocks are the most common sites though any region may be attacked.

Etiology.—The direct cause is *S. pyogenes aureus* though other microörganisms may be present. Predisposing causes may be general or local. They may follow any of the exanthemata, typhoid fever and other general exhausting diseases or be induced by scratching in scabies, pediculosis, eczema or other itching dermatoses. A protracted course may be continued through auto-inoculation.

Pathlology.—The essential changes are the result of the reaction of the tissues to the toxins of the invading microörganisms. The walls of the hair follicles and the perifollicular tissues are extensively infiltrated with leukocytes and staphylococci, the whole mass later undergoing necrosis, producing the core which, upon being thrown off, is replaced by scar tissue. According to Unna, the most frequent method of development of a furuncle is first an impetiginous pustule followed by perifollicular abscess of a lanugo hair and suppuration of the follicle. Opinion differs as to involvement of the sweatglands in the process.

Diagnosis.—The painful character of the lesions together with the formation of the "core" distinguish furuncles from multiple abscesses of the skin of infants, though many writers make no attempt to distinguish the conditions.

Prognosis.—A single furuncle runs its course in a few days and is of no moment. Multiple lesions or a long continued course may affect the general health.

Treatment.—The general treatment is regulated by the findings in the individual cases. Properly selected food is important, and such tonics as arsenic, iron, quinin, strychnin or cod-liver oil may be of value. Local treatment is very important. A single lesion may be treated with hot applications of boric acid solution for short periods two or three times daily to relieve discomfort and promote resolution. A 2 per cent. salicylic ointment should be kept applied over the lesion and for some distance surrounding it to prevent auto-inoculation. If the lesion is seen early, it may be aborted by inserting into the center of the lesion a sharp pointed orange-wood toothpick dipped in phenol. Care must be exercised not to insert this deeply and also to place it either in the early pustule or the pilo-sebaceous opening in the center of the lesion. When general furunculosis is present a daily bath with boric acid solution is advisable. As a rule, nothing is gained by incision of the lesion before the slough is complete.

Carbunculus.—Not seen in children.

(B) DISEASES CAUSED BY BACILLI

Diphtheria of the Skin.*—The symptoms induced by the growth of the Klebs-Löffler bacillus in the skin are not characteristic, but resemble several cutaneous disorders. It has long been known that an open wound might be the site of implantations of this bacillus in which case a false membrane would form accompanied by marked local inflammatory reaction, often with destructive effect, not infrequently terminating fatally or followed by paralyses of similar character to those following the infection as it occurs in the throat or nose.

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*For bibliography to date of publication together with historical, clinical and bacteriologic description, see Knowles and Frescoln, J. A. M.A., cxxiii (1914), p. 398.

In addition to these cases many are now on record where impetiginous, ecthymatous, pustular and eczematous types have occurred, as well as tumors and abscesses. The infection may produce gangrenous patches with severe constitutional disturbance, ulcerative lesions with and without the formation of false membranes, whitlows, and vesicular lesions resembling varicella and dermatitis herpetiformis, and bullous lesions resembling pemphigus. The lesions may occur on any portion of the cutaneous surface though the area about the mouth, ears, scalp, neck and genitocrural region are more often attacked. The disease sometimes runs a protracted course.

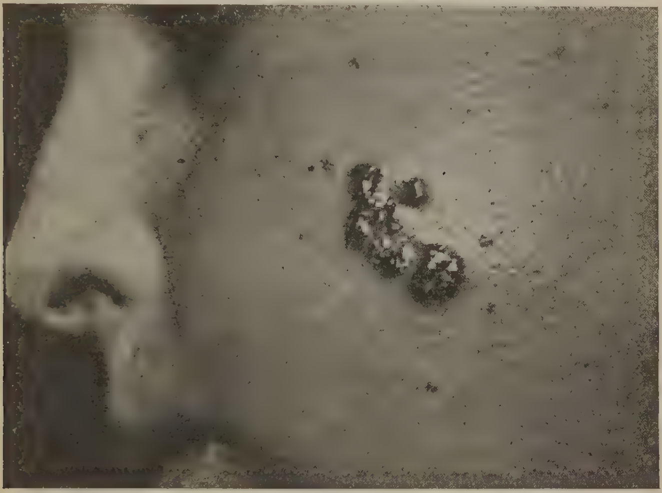

FIG. 21.—Lupus vulgaris incipiens. Boy, aged 12. Since he was 2, when father died of tuberculosis, has had lesion on right cheek which began as a tubercle following injury. Similar lesions appeared near original. Illustration shows dime-sized group of superficial, soft, brownish-red tubercles. Cultures from inoculated guinea-pig gave characteristic growth of human type of tubercle bacillus. (Collection of Dr. Grover W. Wende.)

Etiology.—Children are most often affected though any age is not exempt. The bacilli may be transferred to the skin directly from the mucous membranes of the patient or another infected individual or indirectly through infected clothing or other mediate objects. While *Bacillus diphtheriæ* is the causative microörganism other streptococci and staphylococci are commonly present.

Diagnosis.—The nature of the disease is usually proved by cultural and microscopic examination. Care must be exercised to distinguish diphtheroid microörganisms from the true diphtheria bacillus. Knowles and Frescoln emphasize the distinction in their work.

Prognosis.—With prompt recognition and proper treatment most cases recover. Some terminate fatally in spite of treatment and some run a rather protracted course.

Treatment.—Serotherapy is recommended for cutaneous diphtheria as in the common mucous membrane type. Isolation should be similarly practiced. Local treatment should be carried out in accordance to that recommended for the various disorders it resembles.

Tuberculosis of the Skin.—Tuberculosis of the skin occurs as the result of the local action of the tubercle bacillus in the skin or the action of its toxins brought to the skin from a distant focus. The first group includes lupus vulgaris, scrofuloderma, tuberculosis verrucosa cutis, tuberculosis orificialis, tuberculous ulcers and some cases of erythema induratum (Bazin). The second group includes those disorders now classed under the title tuberculids, and includes lichen scrofulosorum, acne scrofulosorum, erythema induratum, acnitis and folliclis.

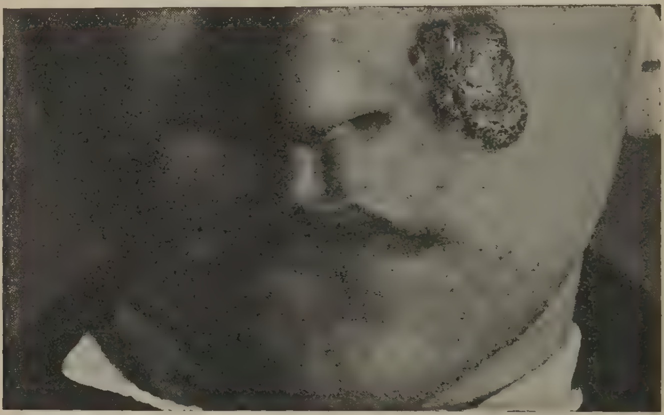

FIG. 22.—Lupus vulgaris. (Fordyce and MacKee.)

Lupus Vulgaris.—Lupus vulgaris is the commonest type of tuberculosis of the skin and is essentially a disease of childhood as most cases begin in this period, but owing to its chronicity it not infrequently persists well into adult life.

Symptoms.—The characteristic lesion is a small reddish-brown, soft, smooth or scale covered nodule beginning, as a rule, about the nose or other parts of the face. The nodules are pinhead to millet seed in size and by development of new lesions patches of varying sizes occur. The increase in size is usually slow and various changes occur. An early patch is well defined, slightly elevated, infiltrated, scale or crust covered, reddish or yellowish-brown in color and devoid of subjective symptoms. Ulceration may supervene producing superficial or deep ulcers with irregular but well-defined margins, and commonly covered by crusts. The floor of the ulcer is reddish or purplish in color, indolently granulating, uneven, occasionally hemorrhagic and at a later date shows beginning cicatrization. The crusts vary with the degree of secondary pyogenic infection and the depth of the ulcerative process. In time a lupus patch may show all the true characteristics at once: An advancing brownish-red scale or crust-covered nodular portion, ulceration with crusting and scar formation. In certain cases after absorption of the lupus tissue from the nose the latter becomes shrunken and retracted, the tip becoming pointed, producing the parrot beak deformity. This, however, occurs only in older children and young adults. In addition to this peculiar and characteristic deformity of the nose, destructive effects occur in the cheeks, lips, chin, eyelids, brow, ears, and neck after several years progress of the disease. In extensive involvement of the trunk serpigenous and gyrate configuration is produced by the peripheral enlargement of the early patches occurring coincidentally with central healing. *Lupus mutilans* denotes a variety attacking the hands and feet in which destructive effects produce various deformitites. *Lupus hypertrophicus* occurs only in older children and adults and is due to hypertrophy induced by the inflammatory irritation. This condition is seen often on the nose. The mucous membranes of the nose, mouth, and throat are occasionally involved. This occurs late through extension of the process initiated early as above described. In these areas the lesions are papillomatous or granulating patches with well-defined borders and present a dull red, pallid, or dirty grayish surface.

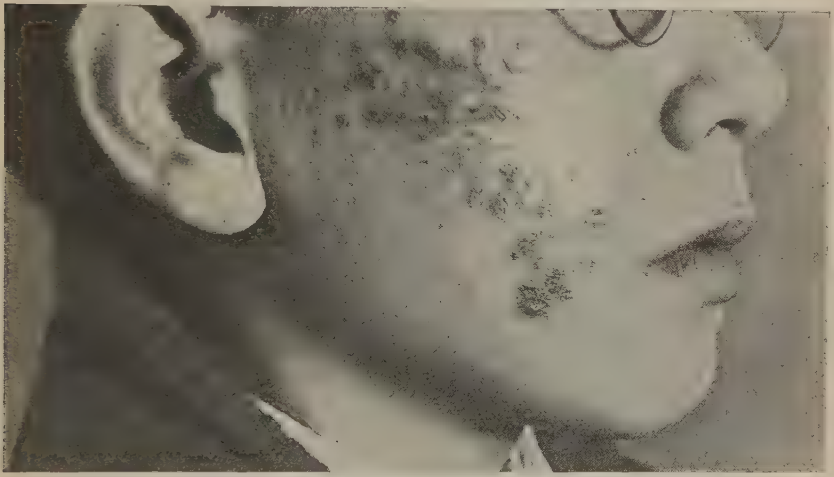

Fig. 23.—Lupus vulgaris. (Fordyce and MacKee.)

The various clinical pictures presented in different stages were formerly all designated by a specific descriptive term. Among the most important are the following: *Lupus maculosis* or *planus; lupus exfoliativa, psoriasiforme,* and *lupus psoriasis; lupus nodosus, tuberculatus, elevatus, tumidus, non-exedens;* and *non-ulcerosus; lupus hypertrophicus, papillosus, edematous, elephantiacus, tumidus,* and *exuberans.* Of these no further description is necessary other than given above.

An important variety limited to children is a rapidly spreading form commonly following an attack of measles. This is described under the title multiple disseminated lupus vulgaris. In this variety multiple patches develop suddenly over various parts of the body, particularly over the elbows, about the knees and other areas. These consist of small discrete nodules or patches varying in size from split-pea to small coin or larger. The patches are made up of typical lupus nodules and are either psoriasiform or verrucous in type.

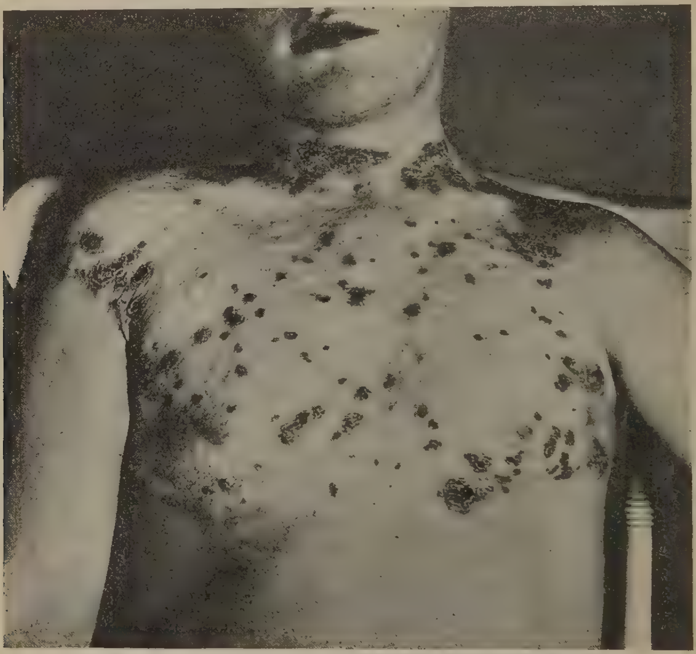

FIG. 24.—Lupus vulgaris. (Fordyce and MacKee.)

Etiology.—The direct cause is the bacillus tuberculosis. Lupus vulgaris occurs most commonly in public practice in patients with poor hygienic surroundings. Frequently a member of the family who is suffering with pulmonary tuberculosis disseminates the causative microörganisms about the home, thus giving opportunity for infection. Picking the nose and scratching the face in this class of children opens the door for infection. Lupus vulgaris has followed vaccination. In the disseminated variety of lupus it is supposed that the bacilli are liberated from a localized focus during an attack of measles, which this variety usually follows, and are spread through the blood stream to various parts of the cutaneous surface.

Pathology.—The chief and characteristic feature in lupus is the nodule which is located in the corium. The epidermal changes are secondary. The lupus nodule consists of one or more giant cells surrounded by small plasma cells and these in turn by connective tissue cells. There are no blood-vessels and no collagen and elastin in the nodule. In the nodular type there is a limiting capsule of collagen about the nodule while in the diffuse variety the cells are diffused evenly over a broad surface producing an even unbroken brownish infiltration. Over the nodule the epidermis is thinned and the normal rete pegs are flattened while at the edge elongation by down-growth of these pegs is noted (acanthosis). In the warty variety hyperkeratosis is added, producing thickening of the horny layer which gives the warty appearance. Acanthosis is more marked in this type. The scar after healing of the lupus nodule is pronounced on account of the complete destruction of connective tissue elements in the nodule. Tubercle bacilli are sparsely distributed in lupus and are usually found in giant cells. The latter are of the Langhan type. When ulceration has occurred leukocytes are added to the infiltrate.

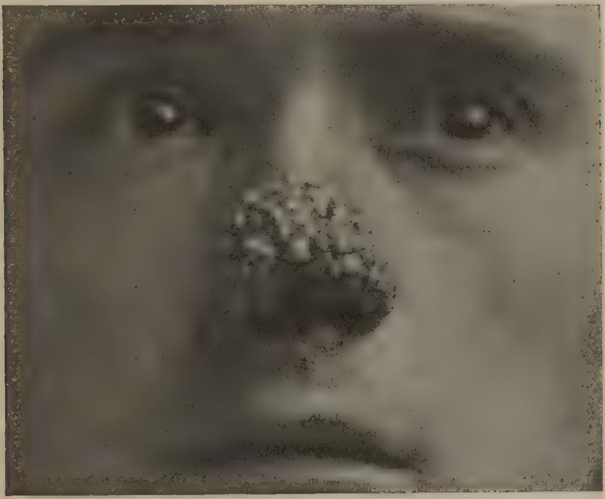

Fig. 25.—Lupus hypertrophicus. (Collection of Dr. Grover W. Wende.)

Diagnosis.—Lupus vulgaris is rare in this country. Its early recognition is important as eradication when small leaves but little disfigurement. Unrecognized the lesion gradually enlarges and destroys vital tissues and its complete eradication becomes more difficult. When crusted early the lupus nodule may be mistaken for impetigo. Its chronicity and persistence in spite of treatment should arouse suspicion as to its nature. Under the diascope the typical apple-jelly-brown color reveals its character. Later when more destructive effects have occurred it may be mistaken for syphilis. The latter rarely attacks children in this form. The nodular syphilid advances much more rapidly, healing as it advances and leaving the usual delicate scar. A nodular and crusted lesion slowly progressing, presenting activity in all portions for several years, is characteristic of lupus and rarely, if ever, seen in syphilis. In older cases, especially of the serpiginous variety, syphilis is strongly simulated. But here again the slow progress together with the presence of the typical apple-jelly-brown nodule and negative Wassermann reaction solve the problem. Epithelioma in the adult is frequently erroneously considered to be lupus. The pearly margin, hard rolled edge and absence of soft nodules, together with the age of incidence, clearly differentiate the two.

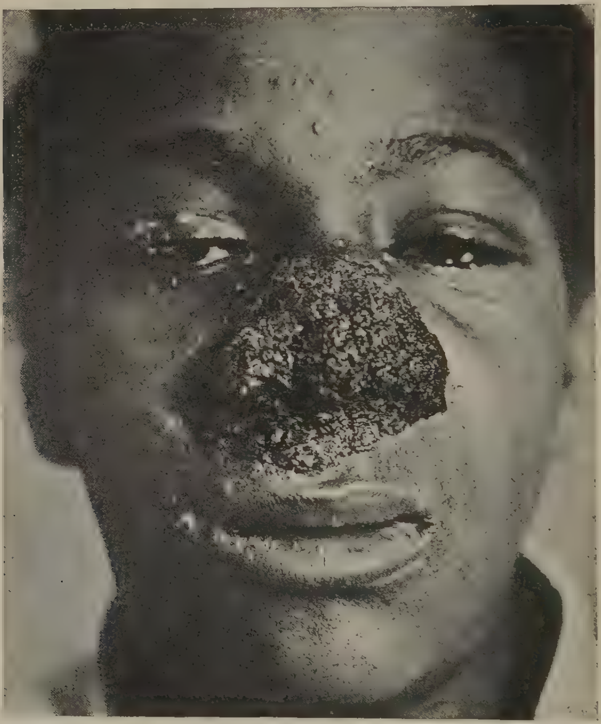

Fig. 26.—Tuberculosus verrucosa cutis, girl. (Fordyce and MacKee.)

Prognosis.—Lupus vulgaris is curable but is chronic, resistant to treatment and frequently leaves disfiguring scars.

Treatment.—There is no simple method of treatment applicable to all cases. The size of the lesion, age of the patient and particular variety presented must determine the method of treatment. The principal object is the destruction of the nodule. This is accomplished by chemical and mechanical agents and general therapeutic measures. In all cases good food, proper air and other measures required to improve the general health are of prime importance. Frequently much improvement from these alone is noted. Treatment with tuberculin, which was tried some years ago and abandoned, has more recently been used successfully by the newer methods of its administration. Small dosage given weekly over a long period is now recommended. Of local measures phototherapy is the most successful. In the Finsen Institute at Copenhagen where the method is used extensively and correctly the results are brilliant, though slow in accomplishment. In this country this method owing to its expense is not practicable. The best substitute to be had here which in principle acts similarly is the Kromayer or quartz lamp. This lamp is rich in actinic rays and has accomplished good results. Recently Heiberg and With, also Sequeira, have employed electric light baths in the treatment of lupus vulgaris with good results. It is reported that deep lesions not directly exposed to the light undergo resolution through the systemic effect of the treatment. The source of light has been a carbon electric lamp. This method used together with the older Finsen light treatment makes the latter more efficient. Cauterization of small nodules may be accomplished by the actual or electric cautery or by freezing with carbon dioxid snow. In some cases excision by surgical means or curettage may be employed. Pyrogallol in paste, sodium phenate in saturated solution and trichloracetic acid have been successfully employed. Adamson has obtained good results in some cases by the local application of potassium permanganate, and more recently of liquid acid-nitrate of mercury. Recurrences after all these methods are common and treatment must be persisted in to obtain results. Radiotherapy is of some value, but to get results sufficient treatment to cause some reaction is necessary and this is not infrequently followed by telangiectasia in the scar, which is disfiguring. The important factor in all cases is to persist in the treatment until the last nodule has been eradicated.

Scrofuloderma.—Definition.—Scrofuloderma is that form of tuberculosis of the skin in which infection takes place by the direct contiguity of the process from the structures beneath, such as a tuberculous gland, bone, or deeply seated abscess.

Symptoms.—Scrofuloderma occurs commonly in childhood, and the lesions are found chiefly on the neck and face, about the joints and bones, the seat of a tuberculous process. The characteristic lesions are soft nodules, subcutaneous abscesses and variously shaped ulcers. The early lesion is a deep nodule which gradually enlarges, degenerates and becomes soft and attached to the skin which eventually breaks down producing an ulcer that heals and leaves a cicatrix. The typical and commonest form occurs in the neck where infected glands become tumid and are dense or doughy to the touch. The overlying skin becomes purplish and thinned and finally breaks down and discharges a sero-purulent fluid comingled with caseous matter and blood. Sinuses and fistulous tracts are formed which undermine and perforate the skin producing a chronic discharge and the characteristic ulcers. The ulcers are usually linear, or elongated ovals, rarely circular. Occasionally by undermining the surrounding skin large irregular ulcers are produced. The floors of the ulcers are uneven, soft, are covered with pale granulations and secrete a thin watery pus. The edges are undermined, thinned, inverted and of normal color or purplish when covering fistulous pockets. The floors are deeply attached to the subcutaneous tissue and exhibit fistulous tracts extending to the tuberculous foci beneath. The crusts are usually thin, tenacious, reddish or brown and are of the shape of the ulcer. The resulting cicatrices are irregular, corded and depressed and frequently active soft nodules are seen which show the continued activity of the process.

Another type of scrofuloderma which occurs especially in infants and children begins as a subcutaneous nodule over the back, on the extremities or the face in which no connection with a gland, bone or joint can be traced. These lesions soften, approach the surface, break down and rupture and follow the same course as those originating in tuberculous glands. This type was formerly known as scrofulous gummata. At times this type occurs along lymphatic vessels of the lower extremities forming small nut to egg-sized tumors which eventually degenerate, rupture and discharge a thin watery or cheesy pus and terminate in the ordinary scrofulodermatous ulcer. Occasionally about the edge of any of the above described ulcers a typical group of lupus nodules may be found, thus proving the identity of their cause.

Etiology.—Scrofuloderma is caused by the bacillus of tuberculosis, the infection of the skin occurring by direct extension of the tuberculous process from some focus beneath the skin. Secondary pyogenic infection plays an important part here in the production of the ulcers which occur characteristically in this condition. The commonest foci are tuberculous glands of the neck though in some instances tuberculous bones, joints and subcutaneous abscesses are the points from which the infection of the skin originates.

Pathology.—The process originates deeply where a subacute inflammatory condition exists. The glands and periglandular structures involved finally break down into a necrotic mass. These necrotic areas may remain indolent and limited or burrow into the surrounding tissue. Eventually the skin over these masses becomes involved in the process and ruptures, producing the typical ulcer. Experimental inoculations have demonstrated the tuberculous nature of these lesions. Tubercle bacilli are more numerous than in lupus vulgaris. The histology shows a diffuse granuloma consisting of plasma cells, with giant cells at the periphery.

Diagnosis.—The history of a deeply situated nodule which softens, extends upward and involves the skin, which in turn ruptures giving exit to the characteristic discharge, later resulting in ulcers having fistulous openings in the floor, make a characteristic picture.

Prognosis.—In time with careful attention to details in treatment these lesions may be eradicated, always leaving more or less disfiguring scars.

Treatment.—In scrofuloderma the first consideration is the general care of the patient. Good food, proper air and hygienic surroundings are of prime importance. Many cases are purely surgical and demand operative procedure. In large ulcerating areas radiotherapy and treatment with the actinic rays from the quartz light are most valuable. The author has seen many cases of extensive ulceration completely heal in a short time under treatment with the actinic rays from the quartz light. Tuberculin is also of value and in selected cases should be employed in the same manner as in lupus vulgaris. Solutions of pyoktanin blue, potassium permanganate, boric acid, or magnesium sulphate may be employed as dressings during the healing process.

Erythema Induratum.—**Synonym.**—*Erytheme indure des scrofuleux* (Bazin).

Erythema induratum is a chronic disease of the skin occurring commonly in the second decade of life, characterized by the formation of nodules deeply in the skin, ulcers, and scars found usually in the posterior portions of the legs.

Symptoms.—Besides the common type to be described here and which is tuberculous in nature, two others have been described in the past. In one of the latter the disease occurs in older people and, in addition to those on the legs, lesions are seen on the thighs and other portions of the cutaneous surface. In these the lesions are more painful, more amenable to treatment, and are probably due to vascular disturbances. A third group is included in the sarcoids.

In the beginning, in the common variety, one or several deeply seated nodules occur in the hypoderm. They gradually enlarge and extend to and involve the surface, break down and produce ulcers, or undergo absorption leaving atrophic areas. Early the nodules are hard and uncolored and can be readily felt with the palpating fingers. They later become colored red or bluish-red, soften and often ulcerate. They vary in diameter from ½ to 1 in. or more. Occasionally node-like patches are present. They may be few or many in number and are usually symmetrically placed. The ulcers are irregular, ill-conditioned, have puriform contents and tend to heal slowly, leaving scars. At a given time all stages may be seen, nodules, ulcers, atrophic areas and scars. Subjective sensations are mild. Some pain and tenderness is present when the stage of ulceration has been reached.

Etiology.—The disease occurs most commonly in young girls and is comparatively rare. Shop girls, who stand much, are predisposed to the disorder. It has been observed in connection with tuberculosis of the skin in other parts of the cutaneous surface, in association with tuberculids of the papulonecrotic type and in persons having tuberculosis in regions of the body other than the skin. The disorder occurs more frequently in the cold seasons and in subjects with poor peripheral circulation. The tubercle bacillus is the direct cause in the common type.

Pathology.—Recent studies place the disease in the tuberculous group, though tubercle bacilli are difficult to find and inoculation experiments are frequently negative. A granuloma consisting of plasma and giant cells is usually found.

Diagnosis.—Erythema nodosum and syphilis must be differentiated. In the former the lesions are more acutely developed, have a more vivid color, are tender and painful, are often accompanied by elevation of temperature, joint pains and other constitutional dusturbances; they never ulcerate and are unaccompanied by scars. The gummatous syphiloderm occurs, as a rule, asymmetrically, the ulcers differ in character, and other signs of syphilis including a positive Wassermann reaction may be found. The therapeutic test may also be applied.

Prognosis.—With proper treatment the disorder yields, leaving only atrophic areas or scars as relics.

Treatment.—The general tonic treatment indicated in tuberculosis should be employed. Rest in bed with elevation of the limbs is recommended. Bandaging before ulceration and local antiseptic dressings when ulcers are present should be employed. Tuberculin injections are highly successful in these cases.

Tuberculosis Cutis Orificials (Tuberculous Ulcers).—This variety of cutaneous tuberculosis occurs rarely if at all in children and therefore needs only brief mention. In this type ulcers occur about mucocutaneous orifices in the subjects of internal tuberculosis. The adjacent mucous tract is the seat of miliary nodules and the ulcers are indolent, oval or circular, shallow, discrete, reddish-yellow in color, having granulating floors and covered with thin crusts. As a rule they are small and show no tendency to heal.

Tuberculosis Verrucosa Cutis.—This is essentially an inoculation tuberculosis and occurs usually in adults. A warty variety of tuberculosis of the skin occurs, however, in children, but is not the type belonging under the title above given. The warty type in children is of endogenous origin and is essentially a variety of lupus and commonly follows an attack of measles. This has already been described under lupus.

In children an *acute tuberculosis* is described in which macules, vesicles, bullæ, papules and pustules form which terminate in deep-crusted, circinate lesions accompanied by caseation of the neighboring glands. In these the tuberculous nature of the lesions has been demonstrated by inoculation experiments.

Exanthematous miliary tuberculosis of the skin occurs in children following the exanthematous diseases. Here the lesions are multiple, indolent, dull, brownish-red, acuminate nodules which degenerate leaving rounded, circular, or polygonal sharply defined ulcers having a violaceous border, an irregular granulating floor and a scanty sero-purulent discharge. Miliary nodules occur both on the floor of the ulcerated surface and about the periphery of the lesion.

Tuberculids.—Synonyms.—Toxituberculides (Hallopeau). Paratuberculoses (Johnston).

Under this title Darier grouped several cutaneous diseases which previously had been considered distinct entities. The early contributions of Hallopeau, Johnston, Colcott Fox and others definitely placed these diseases in the tuberculosis group. Their position has been the subject of much research and, until comparatively recently, they have been considered to be produced by the toxins of Bacillus tuberculosis brought to the skin from a distant focus, rather than by the local action of the bacillus. Notwithstanding the fact that most of the research work done has resulted negatively in respect to finding the bacillus, opinion is gradually changing until it is believed by many that most of these disorders are examples of tuberculosis modified by varying conditions, The experimental work by Rist and Rolland and Lewandoski appear to show that tuberculids are due to the local action of tubercle bacilli which are brought to the surface from a distant focus through the circulation. The baccilli are supposed to be soon destroyed by immune substances formed in the individual by the earlier deep foci.

The subjects of tuberculids as a rule have either demonstrable tuberculous foci or antecedents. The histopatho-pathology is that commonly seen in tuberculosis, though at times only a simple inflammatory process is found.

The members of the group considered in this text are lichen scrofulosorum, acne scrofulosorum, acnitis, and folliclis.

Lichen Scrofulosorum.—Definition.—Lichen scrofulosorum is a disorder of the tuberculous characterized by indolent inflammatory papules occurring in groups, found chiefly on the trunk, and of frequent occurrence in children.

Symptoms.—The disorder was originally described by Hebra as one found in the scrofulous. The disease may be present for some time unobserved as it is not accompanied by subjective symptoms and its objective lesions are not pronounced. The lesions are small, dull-red or yellowish or brownish-red papules, situated about hair follicles. They are grouped, forming patches of varying diameter. Usually the patches are coin-sized. Often a crescentic outline is produced by the arrangement of the papules. Moderate scaling occurs and occasionally a papule is capped by a small pustule. The lesions are limited, as a rule, to the trunk. The course of the disease is slow, often lasting for years, and has a tendency to recur. Upon undergoing involution pigmentation is left, but no cicatrices are seen.

Etiology.—All agree as to the tuberculous nature of the disease. Opinion differs as to whether the eruption is due to the local action of the tubercle bacillus in the lesion or to its toxins brought from a distant focus. It occurs in poorly nourished children, the subject of tuberculosis of the glands, bones or pleura. It has been seen, however, in the absence of these conditions.

Pathology.—Tubercle bacilli have been found in the lesions by a few observers and occasionally animal experiments have been positive. More often both of these findings have been negative. In some cases a tuberculous plasmoma consisting of giant, plasma, and connective cells has been demonstrated; in others merely a subacute inflammatory folliculitis and perifolliculitis. Jadassohn obtained positive reactions with tuberculin in 14 out of 16 cases. He furthermore has seen the disease disappear under these injections. On the other hand, several observers have seen an eruption identical with lichen scrofulosorum produced by tuberculin.

Diagnosis.—From the follicular syphiloderm, which it resembles, the chronicity, absence of concomitant symptoms and the rarity of this luetic eruption in children make the differentiation. From lichen spinulosis it is distinguished by the fact that the lesions of the latter are keratotic and occur chiefly on the limbs, are less inflammatory and are not associated with tuberculous conditions. Lichen planus is readily differentiated.

Prognosis.—This disease readily responds to proper treatment.

Treatment.—Hebra originally advised cod-liver oil internally and externally. In any case proper general care together with mildly antiseptic local treatment soon effects the removal of the lesions. A 2 per cent. salicylic acid ointment is usually efficient.

Acnitis.—Synonym.—Acne agminata (Crocker).

Acnitis is now classed as a tuberculid of the papular type. It presents the general characteristics of this group and very closely simulates folliclis, except in the distribution of lesions.

Symptoms.—This type of tuberculid rarely attacks children, but it is frequently seen in young adults. The lesions are largely limited to the face, though occasionally a few are irregularly distributed on other cutaneous portions. The characteristic lesion is a small, dull red or waxy papule or nodule frequently capped with a vesicle or vesico-pustule. The early lesion begins under the skin, and is colorless. It gradually involves the skin, becomes dull red, and produces the lesion above described. They vary in size from that of a pin's head to that of a hemp seed, rarely larger. Some of the lesions undergo involution without sequel, others become crusted and terminate in small scars. The lesions tend to be grouped in special areas. The forehead, chin, and cheeks are sites of predilection. The course of the disease varies. Individual lesions may clear up in a few weeks, but through constant development of new ones, the course may be prolonged.

Etiology.—While most observers have believed that the disease is the result of the toxins of the bacillus of tuberculosis, the active focus being at a distance, others regard it as a true tuberculosis of the skin, while still others have found it entirely disconnected with that disease.

Pathology.—The histology as described by various observers differs widely. The presence of giant cells and general architecture of the tuberculous process has been frequently recorded. Schamberg found giant cells, but was not convinced of their being significant of tuberculosis. He considered the disease to be non-tuberculous, but was of the opinion that his sections suggested a parasitic granuloma.

No tubercle bacilli have been found in the lesions of this disorder, and animal experimentation has been negative relative to tuberculosis.

Prognosis.—The disorder terminates favorably under proper treatment. When neglected, however, the course may be protracted, covering a period of years.

Treatment.—Given under folliclis.

Folliclis.—Folliclis is now classed as a papulo-necrotic tuberculid, and is classical of this type. It is of frequent occurrence in childhood and is commonly associated with other types of tuberculosis.

Symptoms.—The lesions of this disorder closely resemble those described as occurring in acnitis. They, however, run a more rapid course. The common lesion is a crusted papule or nodule. Early in its development it presents a reddened area upon which develops a vesicle or pustule. This desiccates, producing a crust, which later is replaced by a small scar. The lesions commonly remain discrete though patches are occasionally formed. The course of the disease is variable, individual lesions undergoing complete involution in the course of from four to six weeks. Through the constant appearance of new lesions the disorder may last for years. The sites of predilection are the forearms, hands, legs, and feet. On the fingers the lesions are usually firm, indolent nodules, having a hard center surrounded by a rim of pus. It is probable that the disease described by Crocker under the title acrodermatitis pustulosa hiemalis is identical with folliclis.

Etiology.—The disorder is of common occurrence in children having other foci of tuberculosis. Hempelmann found tuberculids of the papulo-necrotic type in 30 infants under two years of age, in a series of 130 affected with pulmonary tuberculosis. The disease is not infrequently associated with other types of tuberculid. Other factors that predispose are poor peripheral circulation and the cold seasons. The direct cause is either the tubercle bacillus in the situation or its toxins brought from a distant focus, the former in the light of recent work seeming more probable.

Pathology.—Some observers have found the chief pathologic changes about the sweat-glands. Others have demonstrated a tuberculous plasmoma with giant cells and other characteristics of this process. Tubercle bacilli have rarely been found. While the pathology is not clear, in view of the recent experimental work previously referred to, it is quite probable that the disease is of local bacillary origin.

Diagnosis.—The characteristic features of the disease are the successive appearance of papulo-pustular and crusted nodular lesions which terminate in small cicatrices and which are situated largely on the extremities. The individual lesions run their course in from four to six weeks, but through successive development of new ones the disease may last for months or years, and is frequently associated with other forms of tuberculosis. The syphilodermata which might cause confusion are readily distinguished by their course and location, and the coincidental presence of other signs of syphilis.

Prognosis.—With proper care the disease is entirely remediable.

Treatment.—The management of acnitis and folliclis is similar. General treatment is essential in most cases. Cod-liver oil and other tonics, together with wholesome food and proper hygiene, is the first consideration. In folliclis Crocker advised thiol, 5 gr. (0.33) three times daily with applications of 10 per cent. vasogen iodin. Antiseptic washes including boric acid or mercuric chlorid 1:20,000 are indicated. Mercurial plaster or an ointment of ammoniated mercury 1:30 may be employed. Radiotherapy has been useful in cases treated by the author. Tuberculin has been of service in some cases, and valueless in others. Stokes has employed arsphenamin successfully in these disorders.

Acne Scrofulosorum.—**Definition.**—Acne scrofulosorum occurs in infants and children in whom tuberculosis of the glands or other foci of tuberculosis are present. It is characterized by indolent papulo-pustules of anceform type and occurs about the thighs, buttocks, lower part of the back and to a lesser degree on the upper extremities.

Symptoms.—The disease as seen in infants was originally described by Colcott Fox. The lesions are small papulo-pustules which after desiccation become crust-covered. After involution, stains and faint scars remain. According to Fox the early lesion was a small accuminate papule which becomes pustular at its apex, desiccation follows, producing a crust which later falls leaving a superficial crateriform ulcer. After the ulcer heals a small pigmented area or scar remains. The lesions develop both in hair follicles and other situations. Papules simulating lichen planus are occasionally seen, due to flattening of the early papules.

The lesions develop successively over a considerable period of time, and are sparsely distributed. Through this method of development and progress of involution, all stages of the individual lesions may be seen at once. Upon improvement in general condition the disease clears up, but may recur when the vitality is lowered. The sites of predilection are the external aspects of the lower limbs, the buttocks, and the region immediately above. Other areas are less often attacked. The disorder is unaccompanied by subjective symptoms.

Etiology.—The disorder is now classed among the nodular tuberculids. It occurs most commonly in the colder months of the year, and its subjects are of low vitality and frequently present evidence of poor peripheral circulation. Its direct cause is not known, though it occurs definitely among the tuberculous. Tubercle bacilli have not been found in the lesions, and animal experiments have thus far been negative. The presence of glandular and other foci of tuberculosis in these patients suggests the toxic theory of their causation as most plausible.

Pathology.—Histologic examination of the lesions shows circumscribed areas of cellular infiltration, composed of small round cells, connective tissue cells and a few giant cells, about the glands and follicles of the skin, practically a tuberculous plasmoma.

Diagnosis.—Small indolent papulo-pustules situated about the buttocks and above, and on the thighs and arms in a tuberculous infant with a poor peripheral circulation presents a characteristic picture. Lichen scrofulosorum occurs commonly on the trunk and pustules and ulcers are not accompaniments. Impetigo, erythema, and lichen planus are readily differentiated. While the papules of acne scrofulosorum on undergoing resolution resemble lichen planus, their outline is not angular and other classical symptoms of lichen planus are absent. This together with the pustules and superficial ulcers seen in acne scrofulosorum make the diagnosis clear.

Prognosis.—With proper hygienic and tonic treatment together with antiseptic applications, the disease readily yields.

Treatment.—Cod-liver oil and other tonic treatment with proper hygienic surroundings are important factors in treatment. Locally a mild salicylic acid, resorcin, boric acid, or icthyol ointment will control the suppurative lesions.

(C) Diseases Caused by Spirilli

Syphilis.—**Synonyms.**—Lues venera. Morbus gallicus. Pox.

Definition.—Syphilis is a chronic infectious and contagious disorder, acquired or congenital, caused by *Spirocheta pallida* or *Treponema pallidum*, which may attack any tissue or organ of the body, and is characterized by variable symptoms according to the stage of the disorder and the parts attacked.

In this section the disease is described as it occurs in the skin in both the acquired and congenital form. For description of the disease as a whole see volume V, page 611.

Acquired syphilodermata occur in infants and children but rarely, and when they do occur, they present lesions similar in type to those seen in adult life. Infants infected shortly after birth may develop lesions early, especially of the epiphyses of the bones, but taken as a whole, acquired syphilis in children usually runs a comparatively mild course.

Chancre.—The initial lesion in children is usually extragenital in situation and may occur on the lips, face, arms or other situations. It may be represented merely as a dry papule or nodule, or it may be exhibited as an ulcerated lesion. On the lip it may be a large, deeply indurated and ulcerated lesion similar to that seen in the adult.

As stated above, acquired syphilodermata are similar to those seen in adult life, and on account of the rarity of the disorder a full description of all of these lesions would require more space than seems necessary here. An outline of the lesions is all that will be included.

The acquired syphilodermata in children may be classified as early and late. The former are superficial, of symmetrical distribution, run a comparatively short course and disappear leaving no permanent sequels, and are unaccompanied by subjective sensations. The lesions are macules, papules and pustules or combinations of these. The usual eruption is macular, less often some form of papular and very rarely it may be pustular. Mucous patches and condylomata do not differ from these lesions as seen in adults.

Late lesions consisting of nodules, gummata and ulcers are deeply seated, asymmetrically distributed, remain indefinitely in one place or another, and when they undergo resolution leave permanent scars. The size, contour, and other characteristics of these lesions are similar to those occurring in adult life. In children this development is usually restricted, so that the many striking and different pictures presented by these lesions in adults is rarely seen.

Congenital Syphilodermata.—The cutaneous manifestations of congenital syphilis are of the same general character as those of the acquired disease, but certain types predominate. Like the acquired form, they may be divided into early and late, the difference here being that they do not observe so strict a chronological order in their appearance. The bullous syphiloderm of congenital syphilis is fairly common, while bullous lesions in acquired syphilis are rare. The roseola of acquired syphilis, which is common, is not often seen here, a patchy erythema occurring in its place. All observers agree that the palms and soles are very frequently an early site of lesions, some placing bullæ first, others more often see a scaling dermatitis beneath which the surface is red and shining, while others have found maculopapular lesions accompanied by a shiny redness to be of most frequent occurrence. Lesions about the muco-cutaneous orifices are very common and characteristic. Early involvement of the nasal mucous membrane is also common, giving rise to the so-called "snuffles," while involvement of the laryngeal mucous membrane, causing hoarseness or aphonia, occurs slightly less often.

In general, the early cutaneous lesions appear by the end of the third month of life, and as a rule the earlier their appearance the more virulent is the infection. Infants born with lesions often succumb. Most modern observers believe the disease is transmitted chiefly, if not entirely, by the mother and that, as a rule, infection takes place in the latter half of pregnancy. There is much evidence, both clinical and pathologic, to confirm these views.

Bullæ.—These lesions usually occur early, though at time they may be delayed, and their common site is the palms and soles. They also occur on the fingers, toes and extremities, and, exceptionally, are generalized. At times on the palms and soles they constitute the earliest cutaneous eruption. In severe cases they are poorly developed and are represented rather by discs or plaques of macerated epidermis slightly raised by a thin film of serous, sanguineous or purulent fluid. In other instances they may be conical, rounded, flat or flaccid and surrounded by dark red or violaceous borders. In some instances their content is purely hemorrhagic. They terminate by crust formation and healing or by ulceration, shallow or deep, presenting discharging floors. They may be accompanied by maculo-pustules, pustules, genital condylomata and mucous patches of the mouth, nares and anus.

Macules in congenital syphilis usually appear early and they may be discrete or fused into variously sized patches of erythema. The early roseola of acquired syphilis is rarely seen. Erythematous patches variously sized beginning over the buttocks and extending over the back, often involving the thighs, neck, palms and soles, are much more common. These patches are coppery-red or violaceous, well or poorly defined and not infrequently coalesce, forming diffuse sheets of eruption. Desquamation frequently occurs and fissures often form because of inelasticity of the skin due to the infiltration. The soles are apt to be red, shining and desquamating. A fluid exudate which dries into crusts occurs, producing a picture resembling eczema except in the color and subjective symptoms. Rarely a general redness with exfoliation occurs which closely resembles dermatitis exfoliativa of Ritter. In moist regions the epidermis covering the erythematous areas is removed, leaving a red, raw, exuding surface.

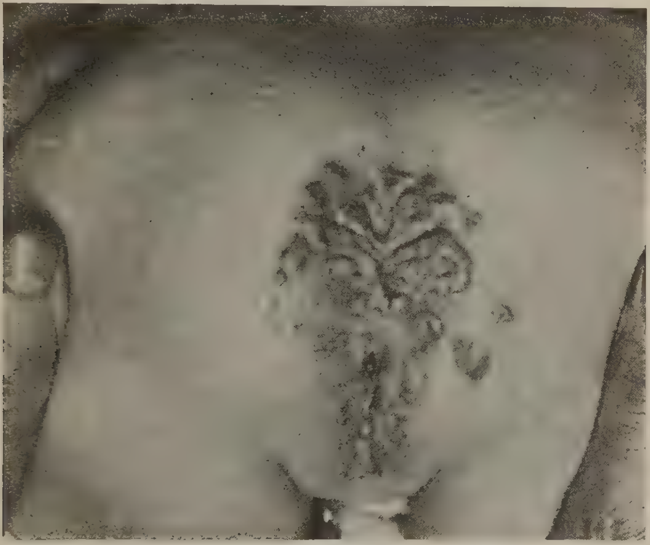

FIG. 27.—Condylomata in a child of 8 months. (Collection of Dr. Grover W. Wende.)

Papules of congenital syphilis may be large or small, flat or acuminate, scale covered or capped with a pustule and terminate in moist situations in condylomata. Acuminate and convex small papules are usually bright or brownish-red and occur chiefly on the limbs. They may be grouped and limited, or extensive in their distribution and may be scale covered or capped with pustules. The small, flat papules are less common, slightly raised and shining, round or irregular, and grouped in irregular patches. More often dark red or violaceous lenticular papules occur, either discrete or agglomerated into patches of infiltration. About the buttocks, face and other regions they are scale covered, while on the palms and soles they form a desquamating, epidermal patch. About the ano-genital region, umbilicus, interdigital spaces, axillæ or other regions where two surfaces come in apposition, they become moist and secrete puriform material. Rarely a large portion of the surface presents moist, secreting papules. By hypertrophy or vegetation these papules become transformed into flat, fissured condylomata coverd with an offensive yellow, or yellowish-white discharge. These vary in size from a small coin to an inch or more in diameter and are elevated in varying degrees above the cutaneous surface. Occasionally they become crust covered or ulcerate. Rhagades frequently occur at the angles of the mouth on a papule or infiltrating erythematous lesion, due to the movements of the affected parts. Opening and closing the mouth becomes painful when these are present. Upon healing they leave linear scars, which are characteristic of the disease.

Mucous patches are constant and common symptoms of the disease, and represent papules of the disease on the mucous membrane, differing from those on the skin on account of the moisture and maceration. They may be pearly-white owing to the detachment of the epidermis and are usually surrounded by a dull red halo, or they may appear as denuded ulcerated surfaces due to the removal of the loosened epidermis in shreds or patches. They may be discrete or confluent, oval or circular, or linear when occurring at the angles of the mouth.

Vesicles in congenital syphilis are among the rarest of cutaneous manifestations. Cases have been described, however, by competent observers which prove the possibility of their occurrence. They are usually conical and are described as being closely set together, and as rising from a violaceous, infiltrated patch. Crocker described vesicles of millet-seed size appearing singly or in groups, with little or no redness at the base, which subsequently developed into bullæ. Grindon described two instances of true vesicle formation observed in congenital syphilis, in both of which the lesions were rather extensively distributed.

Pustules in congenital syphilis occur occasionally. They may be discrete or confluent, localized or, very rarely, generalized. They not infrequently cap the small papule above described. They also occur independent of these lesions. They are not infrequently associated with other manifestations of the disease. They are prone to develop about muco-cutaneous junctions. Occasionally, they are followed by ulceration and crust formation, which terminates in scars. They occur rather frequently about the digits, producing considerable swelling with accompanying deformity, and often induce destruction of the nail substance. Small abscesses resembling furuncles may occur.

They may be few or numerous and are usually characterized by an indolent course.

Nodules and subcutaneous gummata occur late, as a rule, and are very similar to the late lesions of acquired syphilis. In occasional instances their destructive effects are extreme. This is particularly true about the face and genital region. The peculiar characteristics relative to asymmetrical development, color and configuration of the lesions and the sequelæ are all found in these lesions exactly as in the acquired type. The major portion occur after the second year. Rarely, deep and destructive lesions occur much earlier.

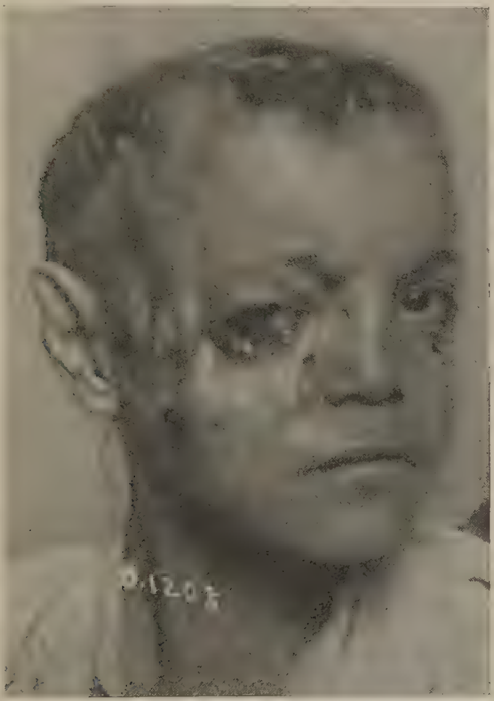

Fig. 28.—Gummato-ulcerative syphilis (congenital).

The patient shown in Fig. 28 began developing nodules and gummata at the age of 11. Deep and destructive lesions followed over a period of 10 years. The skin, subcutaneous tissue and bones were all invaded in this instance.

Occasionally the nodules about the nose are strongly suggestive of lupus vulgaris. The so-called *syphilis hereditaria tarda* merely means that the late lesions of congenital syphilis are delayed over a period of several years in their development. This is frequently true in the cases of acquired syphilis also. It is probable that the early symptoms were so mild as to be overlooked. In the light of modern research there can be no doubt about the position of these late cases.

Diagnosis.—The recognition of congenital syphilis usually presents very little difficulty. A combination of lesions such as condylomata in the ano-genital region, mucous patches and fissures about the angles of the mouth, associated with rhagades and desquamating, infiltrated, erythematous patches on the palms and soles, the characteristic rhinitis and possibly laryngitis, present a picture that occurs in no other condition. There may be only an involvement of the internal organs indicated by marasmus, enlarged spleen and possibly enlarged liver, with the peculiar yellowish appearance and wrinkled condition of the skin and the facial expression of old age in the infant, as the characteristic signs.

Pemphigus and bullous impetigo are readily diferentiated by their being more extensively distributed and occurring in apparently healthy children with no other symptoms, the bullæ of congenital syphilis being, as a rule, limited to the palms and soles.

Eczema and intertrigo are also readily differentiated, the former by the lighter color of the lesions and marked subjective symptoms, the latter by the lessened amount of infiltration of the skin and absence of concomitant symptoms.

Prognosis.—Congenital syphilis is a grave disorder but many infants survive and do well under efficient treatment. Infants born with skin lesions have the least chance. The longer the interval after birth before the lesions develop the better the prognosis. In the later cases severe deformity not infrequently follows and involvement of the central nervous system presents a more or less serious problem.

Treatment.—The former treatment with mercury and potassium iodid has largely been supplanted even in infants by arsphenamin or neo-arsphenamin and mercury. The method suggested recently by Fordyce and Rosen has given excellent results, not only in their hands but in the hands of many others. We have employed it in infants as young as three weeks and in children of varying ages with uniformly good results. They suggest the alternate use of neo-arsphenamin and mercuric chlorid in courses of six to eight injections each. The injections are given at weekly intervals. The mercuric chlorid is employed in palmatin and administered in a dosage of $\frac{1}{10}$ to $\frac{1}{8}$ gr. Neo-arsphenamin is dissolved in freshly distilled water and administered in the following dosage: 0.075 gm. for infants three to eight weeks of age; 0.1 gm. from two to six months; 0.15 gm. from six months to one year, and 0.15 gm. to 0.2 gm. from one to two years. A special needle has been devised for giving these injections, but we have had no difficulty in using the ordinary needle and Luer syringe.

When this method cannot be carried out the treatment by inunction, using 10 to 30 gr. of mercurial ointment three times weekly, applied on the binder, may be employed. Calomel or gray powder in a dosage of $\frac{1}{10}$ gr. to 1 gr. may be given three times daily in milk. Potassium or sodium iodid is indicated in the later cases and in ulcerative conditions, but in view of the very much more efficient neo-arsphenamin it hardly seems justifiable to recommend these drugs at present.

Tonics, however, may be employed and the iodid of iron is of value. It should be given in a dosage of two to five drops of the official syrup, the dosage to be varied according to the age and vigor of the child. With neo-arsphenamin the local lesions soon yield, but in case this drug is not employed it will be necessary to use particular hygienic care for the lesions about the mouth, nares and genital region. Lotions of boric acid, formalin, or mild mercuric chlorid may be employed, as well as soap and water. A dusting powder about the ano-genital region, after cleansing, as above stated, is a valuable agent. In certain of the local lesions a mild (1 per cent.) ointment of ammoniated mercury is of value.

Frambesia.—Synonym.—Yaws.

Definition.—Frambesia is a contagious and infectious disease occurring chiefly in the tropics, characterized by peculiar raspberry or cauliflower-like lesions and caused by *Treponema pertenue.*

Symptoms.—According to Castellani, whose description of the disease is followed here, the disease occurs in three stages with occasionally a fourth. The third and fourth stages may not occur, as in many instances the disease terminates after the second stage. Occasionally lesions belonging to the third stage develop early and are found with those of the second stage. The period of incubation, lasting from two to four weeks, is characterized by general symptoms which include irregular elevation of temperature, rheumatoid pains and headache. The early lesion is a papule which occurs at the site of inoculation and is always extragenital. In a short time the papule becomes moist, and secretes a yellowish material which dries into a crust. Beneath the crust a granulating ulcer forms with sharply defined edges which may heal leaving a white or pigmented cicatrix. At times several papules develop and coalesce and run the same course. Instead of healing, this primary lesion may develop into a large granulomatous lesion (mother yaw) which has characteristics similar to lesions of the later stage. The primary lesion is not indurated and may be accompanied by some pain or itching. Occasionally satellites develop around it before the appearance of the general eruption. Regional adenopathy occurs, the glands being moderately enlarged and hard. The duration of the primary lesion varies from a few weeks to several months and it it usually present when the secondary eruption appears.

The secondary stage begins after one to three months and is accompanied by general symptoms similar to those occurring during the period of incubation. The eruption consists of papules and nodules. The former are small, round and occur on various parts of the body. Some present an apical yellow point or crust. After several weeks some of them regress leaving scaling patches. Others enlarge and coalesce and form patches, while others develop into nodules covered with a yellow crust. Beneath the crust there forms a granulating surface from which a thin purulent material is discharged. These lesions vary from large pea to nut size and are found most commonly on the face and extremities though they may occur on any portion of the cutaneous surface. Like the large, flat papule of syphilis they may clear in the center forming rings, especially about the mouth and anus. Some of the lesions, particularly on the hands and feet, present a verrucous development. Usually in from three to six months in children or from 6 to 12 months in adults, the lesions undergo resolution leaving either hyper- or de pigmented spots.

Occasionally new crops of nodules continue to develop over a period of several years, each lesion lasting two to four months. In addition to the lesions above described, large, irregular ulcers may occur, as well as whitish patches composed of spiny papules.

In addition, the palms are the seat occasionally of hard papules or nodules each having a hyperkeratotic plug in the center. When these undergo resolution, pits remain.

The lesions of the teritary stage are gummatous-like nodules and ulcers. The latter may be irregular, serpigenous with clean-cut or undermined edges, and are frequently fungating. The scars which follow may be thick and irregular and by contracture produce much disfigurement. These late lesions may also attack the bones, but the viscera and nervous system usually escape.

Etiology and Pathology.—The disease is caused by *Treponema pertenue,* discovered by Castellani, and is usually transmitted from one person to another. Children are often infected and in turn infect their mothers. Any open wound may serve as the infection atrium. Castellani believes that the infection may be transferred by flies and other insects. *T. pertenue* is a spiral organism presenting usually from 6 to 20 coils and strongly resembles *Spirochæta pallida.*

McLeod found the following histological changes. In the corium there was a diffuse plasma cell infiltration with some mast-cells, connective-tissue cells and small mononuclear cells, with marked extravasation of polymorphonuclear leukocytes. Collagen and elastin were attenuated in areas of dense cellular infiltration. The blood-vessels were dilated but showed no inflammatory changes in their walls. The appendages of the skin were unaffected. The epidermis showed marked acanthosis, poor development of the transitional layers and both parakeratosis and hyperkeratosis in the stratum corneum.

Diagnosis.—From syphilis it is distinguished by the infrequent involvement of the mucous membranes, lessened amount of glandular involvement and the presence of itching. The papule or nodule of yaws presents a yellow, waxy crust with honey-like serum beneath, which is not seen in syphilis. Yaws is common in children but is never congenital. The Wassermann test is of no value in differentiation as it is positive in both diseases.

Prognosis.—With appropriate treatment the disease is readily controlled. It is more serious in young children and debilitated subjects.

Treatment.—Arsphenamin and neo-arsphenamin are the most efficient drugs in the treatment of the disease. Potassium iodid and tartar emetic are also valuable. According to Castellani, mercury is of little value. He further states that a single injection of neo-arsphenamin will clear up the symptoms and that a course of from three to six injections given at three to six day intervals is usually sufficient to eradicate the disease. Proper hygiene is valuable and local antiseptic dressings are also indicated. In districts where intravenous or hypodermic medication cannot be practiced, Castellani recommends the following: Tartar emetic, gr. 1; postassium iodid, dram 1; sodium salicylate, gr. 10; sodium bicarbonate, gr. 15; water or chloroform water, 1 oz. This amount is given well diluted with water three times daily. One-third or less is given to young children. In recent cases this mixture is reported to be efficient.

(D) DISEASES CAUSED BY VEGETABLE PARASITES

Favus.—Synonyms.—Tinea favosa. Honeycomb ringworm.

Definition.—Favus is a chronic parasitic affection of the scalp characterized by yellowish cup-shaped crusts having a mousy odor, terminating in atrophy or scar formation.

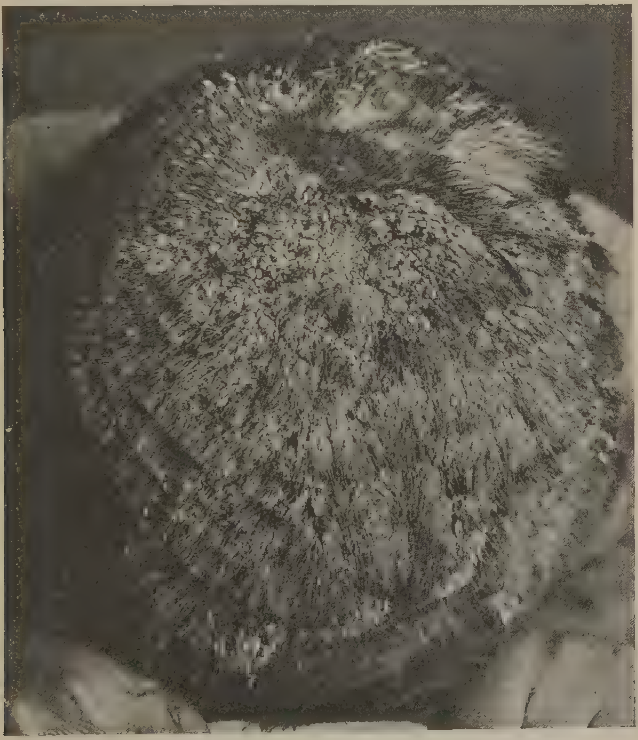

FIG. 29.—Favus, boy. (Fordyce and MacKee.)

Symptoms.—Favus occurs commonly on the scalp but occasionally it attacks the glabrous skin of the body, and the nails. In the scalp the early lesion is a red or yellow spot at the site of a hair follicle. At times a circle of minute vesicles surrounds these spots. In the course of several days the purulent content of these small areas dries and forms yellowish, friable, circular, moderately elevated, concavo-convex crusts. The under surface of these crusts or scutulæ is convex and when removed leaves a cup-shaped depression in the surface of the scalp which is either moist and devoid of its superficial epithelium or dry, red and tender. Each of these unbilicated crusts is usually penetrated by several hairs. As the process extends new lesions form and the older crusts become brown or green through admixture with pus and debris. Occasionally they assume the hue and consistency of dried mortar. The hairs become dry and lusterless but usually not broken. They are easily epilated and finally fall spontaneously, leaving an atrophied follicle. When the disease has been present for some time the scalp presents areas of activity in which hyperemia, pus and crust formation are present and others showing varying grades of alopecia in which atrophy and scars are interspersed about tufts of hair which have escaped infection. As a rule the scalp is involved in areas scattered irregularly over the surface; rarely the entire scalp is involved. Itching is not marked though occasionally it is severe enough to cause scratching, in consequence of which the crusts and scalp are torn. The disease is chronic in course lasting for many years in most cases. Rarely the disease attacks the glabrous skin, when it is characterized by circular patches, with vesicular margins, not unlike

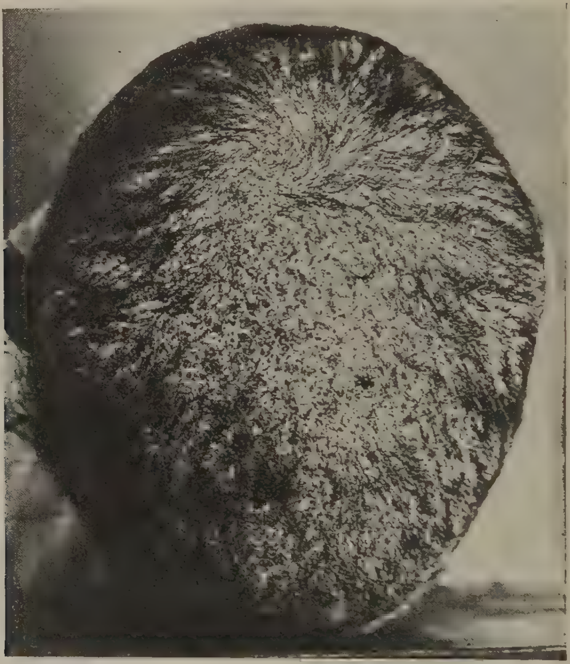

FIG. 30.—Favus. (Fordyce and MacKee.)

ringworm. In these areas typical favus cup-shaped crusts may be seen. These lesions may occur on any portion of the body surface. They are most common on the hands, upper and lower extremities and buttocks. The odor of favus crusts is characteristic and is said to resemble that of mice or the urine of cats. The lesions produced by Achorion Quinckeanum are similar to ringworm and are erythematous and scaling.

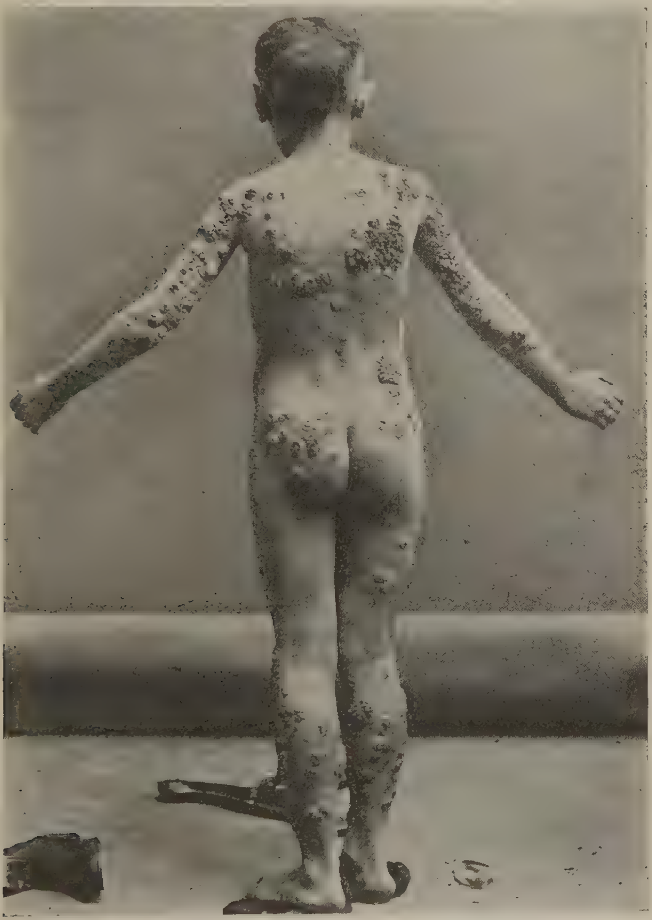

Fig. 31.—Favus corporis. (Collection of Dr. Grover W. Wende.)

Etiology.—Nearly all cases of favus are produced by Achorion Schönleinii (a small number of Achorion Quinckeanum and two other very uncommon varieties). The disease is contageous and usually is transferred from one person to another either by direct contact or through such objects as infected caps, combs and brushes. It is most common in children between 6 and 15 years of age. Geber states the incubation period to be from 6 to 10 days.

Pathology.—The fungus is found in the scales, scutula and hairs. It develops early in the superficial portion of the stratum corneum of the scalp and spreads peripherally and penetrates the hair follicles. An inflammatory reaction follows as indicated by the red spot above described and a follicular pustule. The scutulum is composed of mycelian, spores and a granular debris. In the center spores are abundant while the periphery is composed of dense mycelium which is directed toward the periphery of the cup. Surrounding the scutulum there occurs a leukocytic and plasma-cell infiltration and beneath the cup the fibrous tissue is rarefied. The process destroys the normal structures and scar-formation results.

The mycelia are not abundant in the hairs but can readily be seen, They run parallel with the hair and are composed of jointed cylinders. They divide dichotomously and terminate in a group of spores. "tarsus of favus." The spores also vary in size and shape. They may be round, oval or irregular. They measure from 3 to 7μ in diameter.

Diagnosis.—The recognition of a typical case is not difficult. The sulphur-yellow cup-shaped crusts, irregular bald atrophic areas, together with the dry, lusterless hairs and the peculiar odor present a picture not closely simulated by other diseases. The chief disorders to differentiate are ringworm, psoriasis, dermatitis seborrheica, alopecia areata, lupus erythematosus and folliculitis decalvans. As favus is characterized by atrophic areas, this one symptom would rule out all except the two last named diseases. Lupus erythematosus of the scalp frequently presents atrophy similar to that seen in favus but the disease rarely occurs in children and, furthermore, there are no favus crusts present, and areas are usually found in or behind the ears or upon the face which are characteristic. In folliculitis decalvans, a follicular infection precedes the atrophy, but favus crusts are absent. It also occurs later in life as a rule and in all cases the demonstration of the causative fungus is important.

Prognosis.—Favus is essentially a chronic disease and difficult to eradicate by any therapeutic agent in a reasonable time except by means of roentgen therapy. Many cases last over a period of years, advancing as a rule slowly but certainly.

Treatment.—Roentgen-rays are unquestionably the best remedial agent in favus. A single epilating dose will often eradicate the disorder. The treatment necessarily presupposes proper skill to carry out the treatment successfully. As in ringworm, the scalp is mapped into several areas so as to have the scalp surface treated as nearly at a given distance from the target as possible. Owing to the shape of the head, if a large area is exposed at once some portions will receive more rays than others, owing to the lessened skin distance. Care must always be exercised to properly protect portions of the scalp with lead that are not to be treated. (For dosage see section devoted to ringworm.) Other means include thorough cleansing of the scalp, epilation and the use of parasiticides. Chrysarobin in the strength of 5 per cent. is valuable. Wilkinson's ointment is of some service. Jackson and McMurtry advise iodin crystals 1 dr. (4 gm.) in 1 ounce (3 gm.) of goose grease, as the best parasiticide.

Trichophytosis.—Synonym.—Ringworm.

Ringworm occurs in several forms and the symptoms presented depend upon the location and type of fungus. It is a common disease of childhood and the scalp is the most frequent site. It also occurs on the glabrous skin of the body and on the hands and feet. Its importance in the last mentioned situations has only recently been recognized. The parasitic nature of ringworm was discovered by Gruby in 1842–1844. Furthmann and Neebe in 1891 discovered the fact that two or more fungi were responsible for the various types of the disorder and Sabouraud in 1903 began his researches which culminated in the publication of his monumental work in 1910, in which a great variety of fungi were isolated and properly placed. In this chapter the disorder will be described as it occurs in the scalp under the title trichophytosis capitis; on the glabrous skin as trichophytosis corporis, with subdivisions.

Trichophytosis Capitis.—Synonyms.—Tinea tonsurans. Ringworm of the scalp.

Definition.—Ringworm of the scalp is a contagious disease exhibiting different clinical symptoms, depending on the type of fungus present, and occurs almost exclusively in childhood.

Symptoms.—The common type occurs in well-defined circular patches, variable as to size and number. Occasionally only one small coin-sized patch is present; more often several are seen varying in size up to areas from 3 to 6 cm. in diameter. The patches enlarge by peripheral extension. Each patch is well defined, covered more or less completely with broken stumps of hair, and gray or yellowish scales. Erythema may or may not be present. The stumps of hair which are characteristic are surrounded by a gray sheath for a short distance from the scalp (1 to 3 mm.). This sheath is found on microscopic examination to be the spores of the causative fungus. The affected hairs are readily epilated and through their falling varying degrees of alopecia are produced. Occasionally the infection becomes diffuse, producing a picture like that seen in pityriasis capitis. The hairs are dry, lusterless, friable, and when the finger is passed over them do not resume their former position quickly as do normal hairs. At times a sufficient number of hairs fall to produce a condition simulating alopecia areata. This produces the bald ringworm of Liveing.

Itching in varying degrees is present, but usually is slight. The picture is sometimes changed by trauma when itching is more marked. *Microsporon Audouini* is found in all cases of the type above described. A less common type, the disseminated variety of Alder Smith, occurs in isolated small patches, usually only a few hairs being involved in a group, each hair being broken near its exit from the scalp. When the hair retains its pigment a black dot appearance is presented. The diseased hairs in this variety are situated in scaly macules and may be diffusely scattered over the scalp. Most of these cases are caused by *megalosporon endothrix* (*Trichophyton crateriforme*). Occasionally microspora are found.

Tinea kerion (*kerion celsi*) is another less common form in which an actively inflammatory area exists, presenting a semi-globular tumor-like mass, upon the surface of which a viscid, mucopurulent material from the patulous follicles collects. This lesion is not unlike a carbuncle, is boggy and presents pseudo-fluctuation. The hairs loosen and fall early inducing bald areas and the whole surface is red and congested. Crusting is prominent in some areas and subcutaneous abscesses may complicate the process. There is usually but a single lesion, which, however, may be large, though multiple lesions do occur. *Trichophyton ectothrix* is commonly present though at times difficult to demonstrate. The course of kerion is more rapid than the common variety of ringworm.

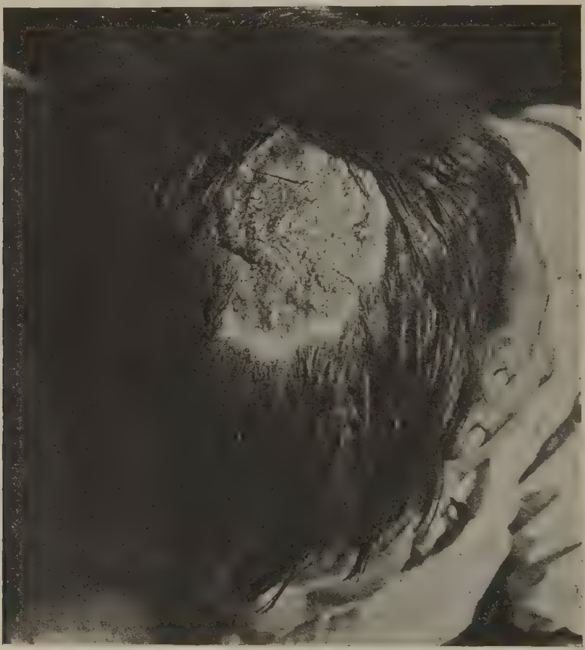

FIG. 32.—Tinea (kerion) girl. (Fordyce and MacKee.)

Etiology.—Ringworm of the scalp occurs in children of both sexes. It is not uncommon to see many members of a public institution affected through the contagious nature of the disorder. It may be transmitted directly from child to child or through the use of infected combs, brushes, wearing apparel, sponges and towels. The most common fungus found is *Microsporon Audouini.* This fungus is almost exlcusively of human origin. *Megalosporon ectothrix* causes most cases of kerion and may be contracted from domestic animals. The black-dot variety is usually caused by *Trichophyton endothrix* which is also of human origin. Through the close contact children enjoy in school and through their habit of exchanging hats and caps the disease may infect a number of children, and for this reason affected individuals are not allowed to attend school.

Diagnosis.—Ringworm of the scalp is distinguished from psoriasis, squamous eczema, and pityriasis capitis by the presence in the former of circumscribed patches of partial alopecia in which broken-off stumps of hair occur which are easily epilated, and by the moderate scaling and inflammatory reaction. In diffuse ringworm some search may be required to detect the affected hairs. A microscopic examination will decide the question. In the three last mentioned diseases the hairs are not broken and remain solidly implanted in their follicles. In alopecia areata the patches are smooth, shiny and devoid of any inflammatory reaction. Short hairs may be present around the margin of a patch of alopecia areata which are likened by Crocker to exclamation points. These are readily distinguished from the scattered, broken stumps seen in ringworm. Favus is distinguished by the presence of yellow cup-shaped crusts, its peculiar odor and the presence, when of any duration, of scar formation.

Prognosis.—Formerly ringworm ran such a protracted course that it was a serious economic question. Schools for such children were established in great centers of population. Many months to some years often passed before the disease was eradicated. In the ordinary type the child recovers spontaneously at maturity. Since Roentgen therapy has been perfected the prognosis is greatly improved, as eradication of the disease is accomplished in a few weeks.

Treatment.—Prophylactic measures include the wearing of a cap constantly to prevent the disease being conveyed to other children. This cap may be made of cloth lined with paper. The latter is changed daily and the cap frequently washed. The treatment with Roentgen-rays has been simplified by MacKee who has devised an indirect electrical method of dosage. He employs a transformer and Coolidge tube and recommends as an epilating dose the following factors: Milliamperage, 2; skin distance, 8 in.; spark gap, 6 in.; time, 3 minutes and 45 seconds. In extensive cases the scalp is divided into several segments so as to have a comparatively flat surface irradiated at once. The portions not treated are protected by lead. About two weeks after the treatment the hairs fall and with them the fungus is eliminated. The hairs regrow as a rule within two months.

Chrysarobin in the strength of 5 per cent. is probably the best local measure aside from Roentgen-rays. This is vigorously rubbed in daily for several days, then a soothing ointment such as a 3 per cent. ammoniated hydrargyrum is used for two weeks. Care must be exercised not to allow the chrysarobin to get into the eyes.

Wilkinson's ointment is valuable though less efficient. Its formula follows:

℞.	Creta preparata	3	33
	Sulphuris sublimat	8	
	Ol. Rusci	8	
	Saponis mollis	15	
	Adipis	15	

M. ft. ungt.

Ointments containing ammoniated hydrargyrum 10 per cent., salicylic acid 3 per cent., or sulphur 12 per cent., may be used but are less valuable. Small patches may be successfully managed by epilating all the affected hairs.

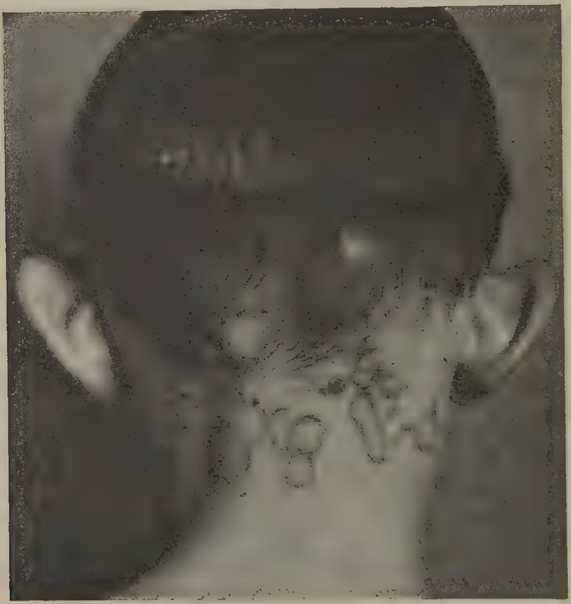

Fig. 33.—Trichophytosis corporis, boy. (Fordyce and MacKee.)

Trichophytosis Corporis.—Synonyms.—Tinea circinata. Ringworm of the body.

Symptoms.—Ringworm of the glabrous skin occurs in two forms. The dry or macular or erythematous form is characterized by circular erythematous scaling areas which spread peripherally and whose centers clear as the margin advances. There may be only one patch or large numbers may be present. The inflammatory reaction is usually mild especially when the lesions are situated on the face or neck. Early the lesions are small but in time may become several inches in diameter. The apparently clear center with a red and scaling advancing border suggested the title "ringworm." Itching and burning sensations are present usually only to a moderate degree. The moist form also occurs in circular patches that develop in the same manner but in these vesicles and pustules are the primary lesions. Early a small group of vesicles or pustules form, around which new rings of similar lesions develop, while the older lesions dry, forming crusts and scales which disappear leaving a clear center. Occasionally several concentric rings are present in varying grades of involution and evolution. Upon the complete involution of the lesions a transient pigmentation may occur. This type is more actively inflammatory and accompanied by more marked subjective sensations. Itching at times is severe.

Guth described an unusual form of ringworm of the glabrous skin in children occurring in association with kerion of the scalp. He noted two forms: One characterized by bright, bluish, or pale-red follicular papules having horny spines, the other by patches resembling psoriasis or dermatitis seborrheica. The lesions were situated chiefly on the trunk and legs. The causative microörgansim in these was found to be *Trichophyton gypseum.*

Etiology.—The disease is contagious and transmitted directly by means of wearing apparel. Domestic animals frequently transmit this form and at times cause small epidemics. The dry type is usually caused by *Trichophyton endothrix* and the moist type by *Trichophyton ectothrix.*

Diagnosis.—Ringworm of the body may be confused with psoriasis, dermatitis seborrheica, eczema, syphilis, and pityriasis rosea. Psoriasis occurs in circular patches with clear centers but it is likely to be more extensively and symmetrically distributed, is less inflammatory, selects regions not invaded by ringworm, is chronic, presents dry, shiny, imbricated scales and is more deeply situated in the skin. Dermatitis seborrheica attacks the center of the body over the sternum and the area back of the ears. The scaling is greasy and vesicles and pustules are absent. It is less inflammatory and the subjective symptoms are usually less marked. All forms of eczema present more infiltration of the skin, more itching, less well defined lesions and no evidence of contagion. The annular types of syphilis are more deeply seated, usually destructive, and usually a history of early lesions can be obtained. The complement-fixation test will be corroborative. Pityriasis rosea is an acute, much more extensive and symmetrical eruptive disease. Is not characterized by vesicles or pustules and the lesions are tawny-yellow and usually unaccompanied by subjective symptoms.

The microscopic examination with demonstration of the fungus in the scales of ringworm always settles the diagnosis. This is accomplished by scraping some scales from the affected area and placing them in a 10 per cent. solution of potassium hydroxid on a glass slide. A cover slip is placed over this and with a medium high power lens the fungi are readily demonstrated.

Treatment.—Small patches are readily cleared up by painting the area each day for from three to five days with a 2 to 5 per cent. suspension of chrysarobin in traumaticin. This induces a moderate reaction which subsides in a few days. A 1 per cent. ammoniated hydrargyum ointment may be used during the reaction. The topical application of tincture of iodin is usually effective. In very young children the tincture of iodin should be reduced 50 per cent. On the face and neck a solution of mercuric chlorid 0.066 in 30 c.c. of water is efficient, or a 3 per cent. ammoniated hydrargyrum ointment may be used.

Eczema Marginatum.—**Synonym.**—Tinea trichophytina cruris.

This type of ringworm was first described by Hebra and occurs usually on the inner surfaces of the thighs, the groin, perineum and the scrotum in males. It may extend over the pubes and backward over the sacrum. The axillæ also are occasionally involved. It is most common in young adults though children occasionally have the disorder. The involved area is red, scale-covered, well-defined and presents a circular or circinate raised margin. Frequently the center of a patch is comparatively free from clinical signs. While erythema and scaling usually represent the clinical picture, occasionally the inflammatory reaction is marked when exudation occurs producing crusting. Itching is present in varying grades, sometimes severe. In the tropics the disease is said to be severe and is often complicated by various secondary invading microörganisms. It is there known as "dhobie (washerman's) itch." The disease is caused by *Epidermophyton inguinale.* In the tropics Castellani has isolated three species of epidermophytons and one trichophyton from these cases.

Eczematoid ringworm of the extremities first described by Djelaleddin Mouktar is another variety of ringworm that has assumed important proportions during the past few years. Many cases of dysidrosis, intertriginous eczema and some of keratodermia are examples of this affection. The disorder occurs on the hands and feet, more often on the latter, and is exhibited in three main types: (1) Acute vesico-pustular; (2) chronic intertriginous, and (3) hyperkeratotic of the palms and soles. The first type is that seen most often in children. In this type the eruptive manifestations appear suddenly, becoming well developed in 24 to 48 hours. The disorder presents the characteristics of acute vesicular eczema or dysidrosis. The vesicles are usually deep-seated and may be diffusely scattered over the entire plantar and palmar surfaces or occur in groups of vesicles, forming patches. After a variable length of time the active inflammatory symptoms subside, the vesicles dry and the process terminates in desquamation. Repeated re-infection may prolong the attack over an indefinite period. Occasionally large areas become denuded of the superficial epithelium owing to the activity of the process. Itching usually is marked and the areas become tender.

The second variety, which is very common in adults, occurs occasionally in children. In this type the skin between the toes becomes white, sodden and fissured. The process extends to the dorsal surface terminating in a more or less well defined margin in which vesiculation may be noted. On the plantar surface the process extends backward beyond the roots of the toes terminating in a well-defined irregular scaling border opposite the head of the metatarsals. The third hyperkeratotic type occurs on the surface of the soles and occasionally on the palms. The chief characteristic is the massing of the stratum corneum in many layers. Occasionally more active lesions (pustules) are interspersed. This type has not been seen in children by the author.

Etiology.—Eczema marginatum is contagious and may be transferred by direct contact or through the medium of clothing. It is a common disorder in young adults who attend gymnasiums. The usual cause is *Epidermophyton inguinale*. The fungi may be transferred from this region to the hands and feet inducing the symptoms above described. Most of the acute types of the latter disorder are also due to the same fungus. Several other fungi have been isolated in the various cases especially in the chronic types. These are usually members of the family of the trichophyta.

Diagnosis.—Eczema marginatum is usually readily recognized. Eczema may be simulated in some cases but a microscopic examination of the scales reveals the fungus and settles the diagnosis. Ringworm of the hands and feet is to be distinguished from eczema and dysidrosis. In all suspected cases a microscopic examination is necessary.

Prognosis.—Eczema marginatum yields readily to treatment as a rule. Ringworm of the hands and feet is more obstinate at times through recurrences.

Treatment.—Eczema marginatum may be treated successfully with the local applications suggested above for ringworm of the body. An ointment suggested by Whitfield for ringworm of the hands and feet containing 5 per cent. of benzoic and 3 per cent. of salicylic acid is efficient but should be reduced to one-third this strength for children.

For the hands and feet the above mentioned ointment is valuable but should be reduced at least 50 per cent. at first. A 2 to 5 per cent. ointment of chrysarobin or the same drug in traumaticin may be employed. In some instances the best results can be obtained by using soothing applications for a short time preceding the active parasiticidal agents. The zinc oxid and liquor calcis or calamine lotion during the day combined with a 50 per cent. naftalan ointment at night accomplish this purpose.

Tinea Versicolor.—**Synonyms.**—Pityriasis versicolor. Chromophytosis.

Definition.—Tinea versicolor is a parasitic disorder occurring chiefly on the covered portions of the skin, characterized by brown scaling macules caused by *Microsporon furfur*.

Symptoms.—The eruption is usually found on the chest and arms. It may extend over other portions of the trunk both front and back but usually is limited in its distribution. The lesions are macules covered with fine scales. They are round, irregular or reticulated pinhead to small-coin size or larger. They are yellowish or fawn tinted or present some shade of brown. Scaling is usually moderate and at times is only evident upon scratching over the surface. Rarely the scales may be adundant and larger. Cases have been recorded, in adults only, where the primary lesion was a follicular papule and others where the lesions occurred on the palms and soles. Mild itching may be present.

Etiology.—The disease rarely occurs in children and then only in older children. It is caused by *Microsporon furfur* discovered in 1846 by Eichstedt. It is only slightly contagious. Sweating appears to be a factor in its development.

Pathology.—The scales are seen on microscopic examination to be largely composed of the fungus. Its appearance is characteristic in that the field shows an interlacing network of mycelial threads with groups of refractile spores interspersed. The groups of spores have been likened to bunches of grapes. For immediate examination scales are placed on a glass slide in a 10 per cent. solution of potassium hydroxid over which a cover slip is placed. Stains are not necessary. The spores vary from 2 to 5μ in diameter and the mycelia about 3μ. While not easily cultivated in artificial media, many observers have produced successful cultures. Several varieties of fungi have been differentiated by Castellani in the tropics.

Diagnosis.—Pigmentary disorders and the macular syphiloderm may be confused with tinea versicolor. Chloasma usually occurs on the face and the lesion is a purely pigmentary one and is not characterized by scaling. The macular syphiloderm also does not scale and moreover other signs of syphilis will probably be present. Other pigmentary disorders are readily ruled out by the absence of scaling. A microscopic examination is at once decisive.

Prognosis.—With thorough treatment the disease can readily be eradicated. Recurrences happen through incomplete removal of the infection.

Treatment.—An efficient method of treatment consists in thoroughly washing the affected area with sapo mollis followed by the application of dilute acetic acid, immediately following which a 5 per cent. solution of sodium hyposulphite is applied so as to have the two come in contact with each other on the skin. When dry a 2 or 3 per cent. sulphur ointment is applied. This method followed for several days is usually sufficient. A less complicated and very efficient application consists in the use of an ointment containing salicylic acid, gr. 15 (1 gm.), benzoic acid, gr. 30 (2 gm.) in petrolatum, 1 ounce (30 gm.). Many other local applications could be employed but the above are usually effective.

Tinea Imbricata.—**Synonym.**—Tokelau ringworm.

Definition.—Tinea Imbricata is a tropical cutaneous disorder produced by a vegetable fungus, characterized by scaling which occurs in concentric lines or diffusely and by its chronic course.

Symptoms.—All portions of the cutaneous surface may be attacked, but some such areas as the scalp, face, palms, soles, axillæ, and nails are less often the seat of the disease. It begins in one or several areas and spreads gradually but continuously. In the early stages patches are seen composed of concentric rings of scaling epidermis. When diffuse, ichthyosis is simulated. According to Manson, the symptoms begin about 10 days after inoculation as a raised brown patch, the center of which breaks, producing ragged scaling with the scales attached at the periphery and free at the ends, pointing toward the center. This circular area spreads peripherally and a new area begins again in the center. This undergoes the same process and extends peripherally, following the first. In this way many succeeding areas occur producing systems of concentric parallel scaling rings which finally become extensive. When the finger is passed over a patch from periphery to center, the surface feels smooth, but when passed from the center outward, the free ends of the scales are felt. The scales are thin, like tissue paper, and may be large, especially over the back. The patches enlarge at the rate of 5 to 10 mm. each week and the rings are about 3 to 6 mm. apart. When the scales are removed, brownish concentric lines are visible on the skin. In older patches the skin is said to present the appearance of clay. The hair follicles are not invaded, but the hairs may fall in the affected areas. The nails, according to Castellani, are attacked and become thickened, presenting a rough surface with deep fissures and scrapings reveal the fungus. Itching is usually marked.

Etiology and Pathology.—The disease is contagious and affects all ages in both sexes. It is endemic in certain tropical countries. Castellani has recently isolated the fungus and reproduced the disease from cultures. He has identified two species of the organism which he terms *Endodermophyton concentricum* and *indicum.* He states that the fungi belonging to this genus are characterized by their growth between the superficial and deep strata of the epidermis, forming an interlacing belt of mycelia which detaches the horny and granular layers from the rete malpighii. Microscopically the fungus presents interlacing mycelial tubes. In hanging-drop preparations, long mycelial filaments are seen but no spore-bearing hyphæ are present. Reproduction is by sprouting, branching taking place.

Diagnosis.—From ringworm the disease is readily distinguished by the absence of inflammatory changes and the presence of the peculiar concentric rings of scaling. Ichthyosis is ruled out by the history and absence of the fungus in the scrapings.

Prognosis.—Temporary relief is readily accomplished by treatment, but the disease recurs indefinitely.

Treatment.—Manson recommends linamentum iodi. Castellani uses, in addition to this, chrysarobin ointment in the strength of 5 to 10 per cent. Also resorcin 8 gm. in 30 gm. of benzoin. Many other agents have been employed with varying results.

Pinta.—Synonyms.—Mal de los Pintos. Mal del Pinto Caraate.

Definition.—Pinta is a parasitic disease of the skin occurring in tropical countries and characterized by variously colored patches due to a variety of fungi.

Symptoms.—The disease begins in a single patch often on the exposed portions of the skin such as the dorsum of the hand and spreads by peripheral extension and by the appearance of new areas induced by auto-inoculation. The patches vary as to size, outline and color. Castellani describes six general types with subvarieties. Black, blue, violet, red, yellow and white are the six main varieties. The surface of the patches is dry and scale covered. In recent cases the scales are small while in older ones the scales become large and thick. Occasionally the patches may be moist or greasy. The hair follicles are not invaded with the fungus but the hairs in affected regions become atrophied and fall. The atrophy is ascribed to a fibrosis of the follicle. The disorder may become extensive and itching in varying degrees is present. Old cases are said to exhale a peculiar musty odor. The palms, soles and nails escape and the scalp is rarely affected. The disease runs a chronic course and may last throughout a life-time. When a patient is affected with several types simultaneously, a striking picture is presented due to the color changes. The red variety may affect the deeper portions of the skin.

Etiology.—The disease occurs at all ages and in both sexes. While seen most often between the ages of 15 and 25 it does occur in children as young as three or four years. Hot, damp climate and poor hygiene favor its development and propagation. The disease is produced by different species of the genera *Aspergillus, Penicillium, Monilia* and *Montoyella.*

Diagnosis.—The disease is distinguished from all others by the peculiar coloration of the patches and by the microscopic demonstration of the various fungi.

Prognosis.—The disease is chronic and tends to persist and recur in spite of treatment.

Treatment.—Castellani suggests chrysarobin in zinc oxid ointment in the strength of 2 to 6 per cent. This, however, cannot be employed on the face. Nor can it be used on extensive surfaces at once. Only small portions can be treated at a time. Sulphur, salicylic acid or resorcin are recommended for the face. In the beginning tincture of iodin, diluted for children, may be used. In Columbia, citrine ointment is a popular method of treatment.

Actinomycosis.—See volume V, page 685.

Blastomycosis.—**Synonyms.**—Blastomycetic dermatitis. Oidiomycosis.

Definition.—Cutaneous blastomycosis is a chronic infectious inflammatory disease characterized by the presence of circumscribed verrucous or papillomatous patches each presenting a sloping red border in which minute abscesses are seen.

Symptoms.—The early lesion is a papule or papulo-pustule which soon becomes covered with a crust. The lesion slowly enlarges peripherally until variously sized areas are formed. When a patch the size of a silver quarter is examined it presents the following characteristics. It is elevated from 1/8 to 1/4 in., is sharply defined, covered by irregular papilliform elevations which are separated by fissures of varying depths which gives the surface a verrucous or cauliflower appearance. At times the papillary projections are fine, comparatively dry and wart-like. At others much secretion is present which dries, forming crusts under which the papillary elevations are larger and lobulated and covered with a sero-purulent secretion. Some of these elevations are very vascular and bleed readily when touched. The margin of the lesion slopes grădually to the normal skin and is red and contains small abscesses filled with a sero-purulent material. These are characteristic of the disorder. The smaller abscesses can only be seen with the aid of a lens and their contents are more serous. Those as large as a pinhead and slightly larger are more purulent It is in these lesions that the causative fungus is found abundantly. As the whole lesion becomes older, portions of it cicatrize leaving a smooth, pink, shiny, delicate scar. Sometimes the scars are irregularly corded but the surface is smooth. At times the scar becomes re-infected as indicated by the development of the small abscesses above mentioned. In certain cases the scars are hypertrophic at first, but later this thickening is absorbed, leaving the smooth, soft, unattached, well-defined, inconspicuous scar characteristic of the disorder.

In time the lesions become as large as a silver half dollar or much larger. In adults patches several inches in diameter are not uncommon. There may be only a single patch or a number may be present. The face and hands are areas of predilection though any portion of the cutaneous surface may be invaded.

Etiology.—The major portion of cases thus far recorded have been in adults, though children may be subjects of the disease. The youngest so far recorded was eight months of age. The essential cause is a yeast fungus termed *Blastomyces.* This apparently gains entrance to the skin through an abrasion or possibly through some preceding inflammatory area.

Pathology.—Blastomycetes are reproduced in tissue by budding and in cultures by mycelial formation. In pus from abscesses and in tissue they occur as round or oval, double contoured, highly refractive bodies. They vary from 7 to 20μ in diameter. Inside the capsule there is a clear space and the body of the organism consists of a finely or coarsely granular protoplasm which frequently contains a vacuole of varying dimensions. Budding organisms in all stages of development are usually present. Both the epidermis and corium show pathologic changes. Marked proliferation of the rete is characteristic, the downgrowths often resembling epithelioma. Miliary abscesses are found throughout this layer and they contain leukocytes, detached epithelial cells, nuclear fragments, epithelial detritus, red cells, blastomycetes and occasionally giant cells. The horny layer is destroyed or extends in thickened masses between the distorted papillæ. The corium is the seat of extensive cellular infiltration consisting of plasma-cells, leukocytes and in fewer numbers connective tissue, mast and giant cells, the last named varying in number in different cases. Tubercle-like nodules are occasionally seen and miliary abscesses are common. Blastomycetes are practically always present in the latter and they are also found between the cells of both the epidermis and the corium and in giant cells.

The organism of blastomycosis grows well on all ordinary media at room temperature and can usually be obtained in pure culture from the small abscesses above described.

Diagnosis.—Verrucous tuberculosis is the principal disease likely to cause confusion. Here the patch is less inflammatory, more dry, less likely to show the sloping bluish-red border and develops more slowly. A rapid demonstration of the organism of blastomycosis is made as follows: A droplet of sero-pus is removed from one of the smaller of the abscesses in the border of the lesion and placed on a slide in a drop of a 20 per cent. solution of potassium hydroxid over which a cover slip is placed. Using a medium-power lens, budding organisms are readily seen. Other disorders to be considered are the rare vegetating syphiloderm, lupus vulgaris and other forms of tuberculosis and coccidioidal granuloma.

Prognosis.—In time cutaneous blastomycosis can be successfully managed. Systemic blastomycosis is grave. This is not described here as it has not been observed in children. For description see Archives of Internal Medicine, August, 1908.

Treatment.—Complete excision of small areas has been found successful. Potassium iodid in as large dosage as possible and continued for some time is often successful. Small areas are also benefitted by roentgen therapy. Copper sulphate is also of value and arsphenamin has been of service in a few instances. Mild antiseptic local dressings are recommended during the period of internal treatment.

Sporotrichosis.—The first case recorded was by Schenck in 1894. A clinical report of a similar case was made in 1899 by Brayton and in 1900 Hektoen and Perkins recorded the third, which clinically and bacterologically was indentical with that of Schenck. In 1903 French reporters began recording cases and from 1906 many cases have been recorded in America and France.

Definition.—The disease is characterized by indolent cutaneous and subcutaneous nodules, abscesses and ulcers originating in an infected wound, usually situated on the hand.

Symptoms.—The early lesion is commonly situated on some portion of the hand or fingers and may be exhibited as a superficial inflammatory discharging ulcer or a nodule. The lesion may resemble an extragenital chancre. Occasionally this primary lesion may be mild and heals before subsequent lesions develop. After a period of a few weeks to three months, nodules begin appearing along the lymphatics of the forearm and arm. They gradually enlarge and may be painful. After some months they become attached to the skin, become red or violaceous, soften and rupture, discharging a grayish-yellow pus. Frequently many of the smaller nodules can be detected by palpation before they become visible. After rupture the lesion may slowly heal or become larger by new fistulous openings occurring around the original lesion. Incision of the nodules may facilitate the growth rather than retard its development. Occasionally the ulcers assume a papillomatous or verrucous appearance suggesting tuberculosis. The number of lesions varies. In a patient five years of age seen by the author, 37 lesions were present on the hand, forearm and arm. The course of the disease is slowly progressive, the lesions often becoming disseminated irregularly over the extremities and trunk. A tuberculoid and a syphiloid type is described owing to resemblance to these disorders. The lymph glands are not attacked, but the mucous membranes, bones, muscular tissue and viscera have all been sites of the lesions.

Etiology and Pathology.—The disease is produced by some species of sporothrix. Castellani and Chalmers describe eight varieties. Unlike blastomycetes, sporothrix cannot be demonstrated in fresh pus nor in sections. The fungus is usually isolated by culture or by animal inoculation. In sections of inoculated animal tissues the organism can be readily demonstrated. The organism gains entrance usually through a wound in the hand or fingers and is disseminated from this primay focus. The disease occurs in the rural districts of France more often than in cities. As the fungus is saprophytic and grows on vegetables among other things, it is supposed the infection may occur from handling or from the ingestion of contaminated vegetables. It has been observed in both sexes and at all ages. The microscopic findings in tissue have been described by De Beurmann and Gougerot as occurring in three types; a lympho-connective tissue or syphiloid type, an epitheloid with giant cells or tuberculoid type, and a polynuclear or ecthymaform type.

Diagnosis.—Tuberculosis cutis and syphilis are most likely to be confused with sporotrichosis and not infrequently the question has to be settled by culture or animal inoculation. Pus or tissue inoculated into the peritoneal cavity of a rat is followed by a characteristic orchitis in which the organism may be found abundantly. Clinically the presence of multiple cutaneous and subcutaneous nodules, abscesses and ulcers, having a linear arrangement over the forearm, preceded by an infected lesion on the hand, is characteristic.

Prognosis.—When recognized and properly treated prompt recovery ensues.

Treatment.—Potassium iodid is specific. The local lesions should be dressed with mild local antiseptic lotions. Darier recommends evacuating the pus and injecting a 1 per cent. solution of iodo-iodid solution and applying this solution to the ulcers.

(E) Diseases Caused by Animal Parasites

Scabies.—Synonyms.—"The Itch." French: Gale. German: Krätze.

Definition.—Scabies is a contagious cutaneous disease characterized by intense itching, most pronounced at night, and by the acarian furrow, vesicles, pustules, and other lesions produced by trauma and caused by acarus scabiei.

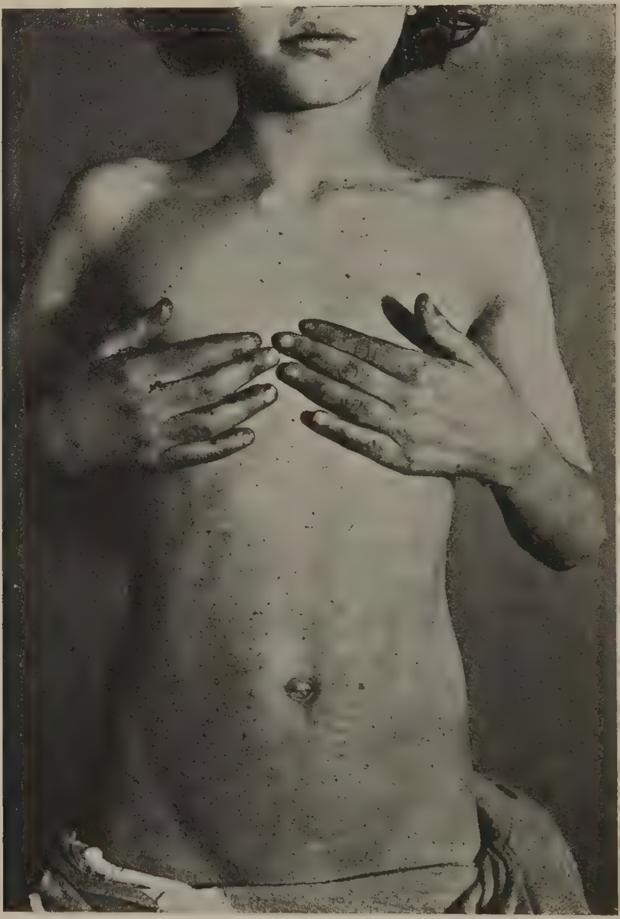

Fig. 34.—Scabies. (Fordyce and MacKee.)

Symptoms.—Scabies is common in children and being contagious becomes essentially a family disease. The lesions found in the order of their importance are the cuniculus or gallery of the parasite, vesicles, bullæ, pustules, excoriations, crusts and in case of long duration stains and pigmentations. The regions chiefly affected in children are the hands, especially on the interdigital surface of the fingers, about the wrists, about the axillæ and breasts, the buttocks, over the genitals in male children and after these regions practically any portion of the cutaneous surface. The face and soles of the feet are attacked in infants, regions seldom if ever attacked in older people. The face becomes infected in nursing infants from contact with the disease on the mother's breast and the feet become involved through the unusual activity of these members in infants. Intense itching is present and may occur only at night. The characteristic lesion is the acarian burrow which in the tender skin of children may become an inch or more in length; ordinarily its length is about ¼ in. This burrow is made by the female acarus as she progresses in the stratum corneum and contains the ova and excrement of the parasite as well as some extraneous debris. It appears as a gray or dark colored thread or ridge and while usually linear it may present curves or be irregular in its course. The dark specks along the burrow are said by Darier and others to be collections of dirt in openings made in the roof by escaping young acari. A vesicle or bulla is usually connected with the gallery. When excised and examined microscopically the acarus is found at the distal end and 6 to 12 or more ova or developing acari are noted along its course. Through scratching and secondary infection various grades of inflammatory reaction are produced. Impetigenous lesions and eczematous patches thus result. Large bullæ, long furrows and marked pustulation are characteristic of the disease as seen in the tender skin of children.

Etiology.—Scabies is produced directly by the *Acarus scabiei* (*Sarcoptes scabiei*) which is transferred from one individual to another by direct contact or mediate objects. It occurs in all grades of society though poor hygiene and filth are factors in public practice. The intimate contact of children in school and play, together with their sensitive skins, probably accounts for the more rapid dissemination of the disease than is the case in adult life.

Pathology.—The female acarus is just visible to the naked eye; the male is smaller. The female only burrows into the skin where she deposits the ova. Acari have oval bodies and eight legs. The four anterior are provided with suckers, the posterior, with bristles. The ova are oval and are placed with their long axes transversally in the cuniculus. Larvæ begin to hatch in from four to eight days and have six legs. They make their exit from the burrow, imbed themselves in the skin, slough their skin and the females after impregnation are prepared to form new cuniculi.

Diagnosis.—The history of the case together with the lesions in characteristic locations renders the diagnosis plain, as a rule. It must be remembered that the disease occurs in the clean as well as others. A history of other people being affected, the presence of the gallery, vesicles, pustules, and other signs of a traumatic dermatitis, these lesions occurring on the hands between the fingers, over the wrists, about the axillæ, buttocks and genital region, with more marked itching at night, make a conclusive picture. To settle the matter, remove a lesion with a sharp scalpel and examine microscopically, when the acarus and ova can easily be demonstrated. In pruritus hiemalis, which is more frequently mistaken for scabies in the middle west in the autumn and winter, the lesions are only those induced by scratching a dry skin. No vesicles and no galleries are found. Here the regions affected are the legs, thighs and body. The hands, wrists and genitals are spared. Itching here is worse when disrobing while in scabies it is worse after retiring. Eczema is distinguished by the presence of patches of weeping dermatitis and not by the discrete lesions above described. Eczema may complicate scabies, a fact to be remembered in this connection.

Prognosis.—When recognized and properly treated scabies readily yields. Unrecognized, it may last indefinitely.

Treatment.—Two simple methods are efficient in the treatment of scabies in children. Sherwell recommended a dusting powder containing sulphur to be applied daily for a week or 10 days, which commonly is all that is necessary. The powder may be dusted in the sheets and over the body under the clothing and be used in the strength of 5 to 15 per cent., depending on the age. The most commonly employed method is to have the patient bathed, preferably in the evening, after which a sulphur ointment in the strength of 5 to 10 per cent., using adeps as the base, is thoroughly applied over the entire surface affected. Underclothing is then put on and not changed until the end of the treatment. Fresh ointment is applied for five consecutive nights without bathing. On the sixth day a second bath is given, clean clothing and a soothing cream employed subsequently. To prevent reinfection all clothing previously worn should be sterilized. Equal parts of olive oil and lime-water, or bismuth subnitrate 4 gm., zinc oxid 8 gm., olive oil 120 gm. and aqua calcis 120 gm. may be used as soothing applications. After soothing treatment for two weeks has been carried out, if any evidence of the original disease remains, another period of sulphur on the affected area may be resorted to. Over treatment is always to be avoided. Should the skin be hypersensitive to sulphur, indicated by reaction, the active treatment should be suspended and the soothing one employed. Balsam of Peru and beta napthol may be substituted in certain cases. Eczematous patches remaining should receive treatment recommended in that disorder.

Pediculosis.—**Synonyms.**—Phthriasis Morbus pediculosis. Tonsuriers. French: Phtiriase, Maladie pédiculaire. German: Läusesucht.

Pediculosis of the scalp is common in children of the poorer classes, and occurs also occasionally in the more cleanly. Pediculosis of the body is rare in children though common in adults. This disorder has been one of the scourges among soldiers of all fronts during the late war. Pediculosis pubis does not occur in children, though the parasite causing this affection occasionally attacks the eyelashes in children.

Symptoms.—Pediculosis capitis is characterized by the presence in the scalp of the parasite, its ova, and various inflammatory symptoms induced by scratching and secondary pyogenic infection. Any portion of the scalp may be involved though the posterior portion is most commonly and more severely invaded. In a proportion of cases the only symptoms noted are the presence of the parasite on the scalp, ova in rows along the hairs and itching of varying grades; usually however, there is added to this the presence of pustules, crusts, excoriations and moist and oozing surfaces. The hair is matted together by the escaped serum and in the mass are found crusts and debris often emitting a distinct odor. The suboccipital glands are frequently much enlarged and impetigo involves the region of the nose and lip due to scratching from reflex irritation. The ova are seen firmly attached to the hairs as whitish or grayish oval bodies frequently extending several inches from the surface of the scalp. Care must be taken to distinguish them from the fatty scales that occur in pityriasis steatoides which not infrequently are pierced by a hair and slightly resemble the ova. Itching is a pronounced symptom in all cases and in long-continued and neglected cases may induce systemic changes.

Etiology.—The disorder is induced by *Pediculus capitis* (head louse). This parasite is grayish in color and measures 1.2 to 3.2 mm. in length and is about one-half as broad as it is long. Its head is provided with two hairy antennæ (each of five articulations) and two eyes. The thorax is narrow and presents six tracheal stigmata and has attached on either side three hairy legs provided with tarsal hooklets. The abdomen is divided into seven segments defined by blackish indentation on either side. The males are fewer in number and smaller than the females. The ova or nits are grayish or dirty-white, oval in contour and are attached to the hairs by a cylindriform sheath of chitin which completely surrounds the hair. The free bulbous end of the ovum projects toward the free end of the hair. They are deposited in series along the hair being gradually removed from the scalp with the growth of the hair. The parasites have great reproductive power. One female is capable of depositing about 50 ova in six days. These in turn hatch in one week and become sexually active in two weeks more. The parasites are conveyed from person to person by direct contact or by mediate objects.

Diagnosis.—An impetigenous or eczematous condition of the posterior portion of the scalp always warrants a search for pediculi. Similarly an impetigo of the lip and about the nose may be the indirect result of pediculosis. Enlarged post-cervical glands with itching in the scalp is always significant. Ova may be distinguished from scales on the hairs by the firm attachment and the oval shape of the former.

Prognosis.—The condition yields promptly on recognition and the institution of efficient treatment.

Treatment.—Petroleum is the parasiticide commonly employed. This may be scented with balsam of Peru if desirable. The entire scalp is saturated with this, including the hairs, and left on over night. In the morning a thorough washing with soap and water is employed, followed by the application of dilute acetic acid or 50 per cent. alcohol to remove the ova. The eczematous or impetigenous conditions are relieved by the subsequent application of a mild sulphur, or ammoniated mercury ointment. Relics of ova may remain which are removed by combing. As a rule it is unnecessary to cut the hair, but at times this procedure has to be resorted to.

Pediculosis Corporis.—Synonyms.—Pediculosis vestimenti. Phthiriasis.

Pediculosis corporis is rarely seen in children. It is a disorder rather of adult life and particularly of the elderly, the poor and cachectic. Crocker states that even in neglected dirty children the parasites are seldom seen. This parasite resembles the head louse, except that it is larger, measuring 1.2 to 4.2 mm. in length. The female is larger than the male. The thorax is separated from the abdomen, which is hairy, yellowish at the margins and provided with eight segments. The eyes are black and prominent in both sexes. The parasites are dirty-white or light grayish except when distended with blood when they become dull red or purple. They live in the clothing and visit the skin only for nourishment. The only characteristic symptom of the disorder is a hemorrhagic spot level with the skin where puncture is made for obtaining blood. A secondary dermatitis is usually present and is characterized by unusually long excoriatious. Transitory wheals, small papules and pus infections may occur and in long-continued cases pigmentations follow. The long series of changes induced in the aged and cachectic and the serous pyodermias that occurred among soldiers in the trenches during the late war will not be detailed here.

Treatment.—Sterilization of the clothing with heat soon terminates the disorder. In adults the body hairs have to be freed of ova. The secondary dermatitis is treated with soothing lotions or ointments such as indicated in acute eczema.

Pediculosis palpebrum is occasionally seen in children and is caused by Pediculus pubis. In this condition the ova are attached like beads on the hairs with the parasite clinging to the hair near its base. The borders of the lids present what appear to be dark crusts which on close examination prove to be the pediculi closely attached to the ciliary margins with their heads imbedded in the hair follicle. The ova are pyriform in shape and smaller than those of the head variety. The removal of the parasites and ova may be accomplished with the aid of small forceps.

Grain Itch.—Synonyms.— Acarodermatitis urticarioides (Schamberg). Straw itch. Barley itch.

Definition.—Grain itch is a cutaneous disorder characterized by an eruption consisting of wheals exhibiting a central pinpoint vesicle. It is caused by *Pediculoides ventricosus,* an itch mite that attacks the skin but does not burrow.

Symptoms.—The disorder begins with the formation of vesicle-capped wheals variously distributed. The clear contents of the vesicle soon become lactescent or puriform, constituting a definite pustule, or in place of wheals the lesions may appear as slightly elevated erythemato-urticarial spots or papulo-urticarial lesions. The lesions are lentil to finger nail in size and are oval, round, or irregular in shape. They are edematous and elevated, from 1 to 2 mm. above the level of the surrounding skin. Their color is a rose tint as a rule though rarely the pinkish-white anemic area seen in ordinary urticarial lesions is seen. The central vesicle or pustule is usually minute, though at times it may reach the diameter of 3 mm. These larger lesions, consisting of an erythemato-urticarial lesion capped with a pustule, strongly resemble lesions of variola. The eruption is commonly profuse and involves the neck, chest, abdomen and back and to a lesser degree the arms and legs. The face may present a few scattered lesions, while the hands and feet are practically free. As a rule the smaller the individual lesion the more diffuse the distribution. It is accompanied by intense itching which is more marked at night. Secondary lesions are those of pyogenic infection induced by scratching. Mild constitutional symptoms exhibited as malaise and anorexia and moderate elevation of temperature, one to four degrees, are occasionally present. In many patients no constitutional symptoms occur. A moderate leukocytosis and eosinophilia was noted in a large number of cases examined by Schamberg.

Etiology.—The direct cause is the mite *Pediculoides ventricosus* which infests straw. The disease occurs in epidemics from May to October. Children as well as adults are attacked when they come in contact with insected straw. Groups of dock laborers or sailors are frequently attacked. In an epidemic studied by Schamberg and Goldberger the infection was traced to new straw used in mattresses, all of which came from the same locality.

Pathology.—Schamberg describes the histologic changes in a typical lesion, a vesico-pustule situated on an urticarial base, as follows: Over the lesion the epidermis is elevated and the stratum corneum is reduced to one or two layers and the stratum granulosum is absent. Two layers of fusiform rete cells extend from the lateral portion of the roof of the vesicle toward the center whence they become lost. Beneath the rete large numbers of leukocytes were present. In the corium there was vascular dilation with edema and a dense circumscribed cellular infiltration consisting of round cells and polymorphonuclear leukocytes, and in the middle and deeper portions of the corium many mast cells were present. There was no evidence in the lesion of the presence of the parasite. Schamberg states further that it is probable that in extracting nourishment from the skin the mite synchronously injects an irritating substance which gives rise to the lesion. *Pediculoides ventricosus* belongs to the class Arachnida, order *Acarina* family, *Tarsonemidœ*, genus *Pediculoides.*

Diagnosis.—The disorder is to be differentiated from varicella, scabies, and urticaria. Its more frequent occurrence in adults, presence of intense itching and the urticarial character of the lesions distinguishe it from varicella. It differs from scabies in the character and location of the lesions. The absence of galleries, of lesions on the hands, and the presence of papulo-urticarial lesions rule out scabies.

The epidemic character, long duration of individual lesions, the accompanying vesication and pustulation, and the constitutional disturbance at once differentiate it from urticaria. A history of coming in contact with straw is a valuable point in all suspected cases.

Prognosis.—The disease spontaneously disappears in time. It may be prolonged by reinfection but when recognized and properly treated disappears in one or two weeks.

Treatment.—This involves the destruction of the parasite and the treatment of the lesions. The former is readily accomplished by disinfecting the clothing by boiling or fumigation with sulphur or formaldehyd. When a straw mattress is the source of infection this may be freed of the parasites by exposure in a closed chamber to steam, sulphur fumes or formaldehyd. For the cutaneous disturbance Schamberg recommends the following ointment: Beta napthol, gr. 30 (2 gm.), sulphur precipitate, gr. 40 (2.66 gm.), adeps benzoate, 1 ounce (32 gm.). This may be reduced in strength for smaller children. Ordinarily with this treatment the itching subsides in from 12 to 36 hours and the disorder clears up within a week to 10 days.

Ixodes.—**Synonyms.**—Wood-tick. French: Pou de Bois; tique; German: Holzbock.

In certain wooded districts in America the wood tick attacks the skin, producing inflammatory reactions. The tick becomes firmly attached to the skin and resists forcible removal. The body of the tick frequently becomes so distended with blood as to appear like a pedunculated tumor.

The beak of the female tick is armed on either side with a maxillolabial projection having curved hooklets. The mandibles also present similar obstacles to forcible extraction of the head. When removal is thus attempted parts of the head remain imbedded in the skin, which subsequently induce irritation. A drop of turpentine or benzine applied to the tick causes it to retract the head and its easy removal is accomplished.

Other insects which occasionally induce cutaneous eruption are gnats, mosquitoes (*culicedæ*), midges (*Chrionomidæ*), bees (*apes mellificæ*), wasps (*vespidæ*) and black flies (*Simulium venustum*). They produce by their bites or stings urticarial lesions, papules, and ecchymoses. Severe cutaneous eruptions are produced on the face, neck, arms and legs of infants and children by mosquitoes and midges.

Treatment.—For the bite or sting aqua ammoniæ or spirits of camphor may be employed. For subsequent lesions a zinc oxid and liquor calcis or calamine lotion is useful.

Brown-tail Moth.—**Definition.**—An eruption consisting of urticarial wheals, minute papules or vesico-papules may be produced in the skin of susceptible individuals when brought in contact with the caterpillar of the brown-tail moth.

Symptoms.—The eruption is seen most frequently during the months of May and June though to a lesser degree it occurs at any season. The inflammatory reaction is the result of the penetration of the skin by the nettling hairs of the caterpillar. These hairs may be brought directly to the skin by the presence of the caterpillar or carried through the air from an infested tree, or be deposited from clothing previously infested. The degree of inflammatory reaction depends upon the number of hairs gaining entrance into the skin. When the caterpillar is crushed upon the skin a severe dermatitis follows. When the nettling hairs are deposited indirectly a more diffuse and milder urticarial rash follows or the eruption may consist of minute papules or vesico-papules. Itching of varying grades accompanies the eruption and may begin in from 20 minutes to several hours after coming in contact with the hairs.

Etiology and Pathology.—Tyzzer has demonstrated that the disease is produced by the penetration of the skin by the sharply pointed, barbed, nettling hairs found chiefly on the caterpillar of the moth. These hairs contain a chemical substance of an irritating nature which produces the reaction. The pathologic process in the skin consists of necrosis of the epidermal cells around the nettling hairs, the formation of microscopic vesicles at the site of injury and inflammatory changes about the vessels in the corium.

Treatment.—Soothing and anti-pruritic lotions and ointments are indicated. Cases are sometimes rebellious owing to the depth of penetration of the nettling hairs.

Pulex Irritans.—Synonyms.—Flea. French; Puce commune. German: Gemeiner Floh.

Definition.—Flea bites in infants and children cause an urticarial eurption accompanied by severe itching in susceptible skins.

Symptoms.—The simplest lesion consists of a reddened ring having a central marking the site of the skin injury. The erythema may be transitory, disappearing in a few hours, or exudation may take place producing an elevated urticarial wheal having the central puncture accompanied by boring and smarting sensations. In severe cases a well-marked petechial lesion is seen in the center of the wheal and secondary inflammatory lesions are added through scratching. The lesions are at times arranged in lines marking the progress of the parasite over the cutaneous surface. It is important to distinguish this disorder from lichen urticatus. In the latter disorder a reddened area centered by a vesicle occurs which on drying presents the appearance of the puncture made by the flea. Careful examination of the lesions should reveal the distinction.

Treatment.—Soothing lotions containing phenol, or alkaline or tarry lotions suggested in ordinary urticaria are indicated. As preventive measures Stelwagon ("Diseases of the skin") advises wearing bags filled with gum camphor or pyrethrum under the clothing.

Uncinarial Dermatitis.—Synonyms.—Ground itch. Mazamorra.

Definition.—Uncinarial dermatitis is an inflammation of the skin of the feet produced by the larvæ of *Ankylostoma duodenale* and *Necator americanus* (Stiles).

Symptoms.—The early symptom is itching occurring between the toes, on the soles and other parts of the feet. The itching is soon followed by redness, tumefaction and the formation of papules, vesicopapules and bullæ. At times more serious grades occur with the formation of pustules and ulceration from secondary pyogenic infection. Recurrences are frequent from re-infection.

Etiology.—The disease occurs in the southern states of America, Porto Rico as well as in tropical countries. The larvæ of hookworm are found in the sand and dirt being originally deposited there in discharges from the intestinal canal of infected individuals. The disease is prevalent in warm, rainy weather and attacks those going barefoot. The dermatitis above described is the initial stage of ankylostomiasis.

Treatment.—In the early stage salicylic acid in collodion one part to six is recommended by Castellani. Antiseptic lotions containing boric acid, phenol and mercuric chlorid are recommended together with salicylated ointments. Castellani recommends the institution of treatment for the general disease at the moment of appearance of the dermatitis which includes the internal administration of thymol, eucalyptus oil, eucalyptol, beta naphthol or male fern.

Creeping Eruption.—**Synonyms.**—Larva migrans (Crocker). Hyponomoderma (Kaposi). Dermamyiasis linearis migrans oestroas (Kurnberg).

Definition.—This disorder, characterized by the formation of a narrow, raised, thread-like line produced by excursions in the skin of the larva of a bot fly, was first described by Lee and Crocker and later in this country by Van Harlingen, Stelwagon and others.

Symptoms.—The characteristic lesion is a slightly raised, thread-like line which extends over the cutaneous surface in an irregular zigzag manner producing loops and other curious configurations. This line may be light or dark red in color and comparatively smooth, or be surmounted by a linear, vesicular formation, or present a beaded appearance. As the lesion becomes older the color becomes darker and may leave pigmentation. The line extends over the surface at the rate of 1 in. or more a day. Moderate itching and burning occur over the site of the organism. In Haase's case migration occurred only at night. The sites of election are chiefly about the feet and buttocks, though exposed portions such as the hands, forearms and lower portion of the limbs may be the starting point from which extensive excursions over the cutaneous surface may be made. Crocker states that the disease is common in children in Arabia and is found frequently in Russia. In this country many cases are reported in the south. A child so infected was seen on Dr. Abt's service in Micheal Reese Hospital, having been sent from Memphis. Hamburger states that the lesion frequently resembles the burrow of *Acarus scabiei.*

Etiology.—The direct cause is the larva of a bot fly *estridæ* of the genus *Gastrophilus* and probable species *Hemorrhoidalis.*

Pathology.—In a histological study of the disease Knowles found the burrow situated largely in the rete. It measured from 0.25 to

0 75 mm. in diameter, contained larvæ, and was filled in places with granular and cellular debris. In areas around the burrow inflammatory changes were present, indicated by dilated vessels and cellular infiltration.

Diagnosis.—The disease is readily recognized by the length of the line and other peculiarities above noted.

Treatment.—The usual treatment is excision of the area about the extending point. Stelwagon used a solution of mercuric chlorid 2 grain to 1 ounce of water applied cataphoretically on an area 1½ in. around the advancing end of the line and touched the suspected site of the parasite with a small quantity of nitric acid. Hutchins successfully treated a case by using a few drops of chloroform.

Craw-craw.—**Definition.**—Craw-craw is a term loosely used by the natives of the West African coast to designate several diseases of the skin. The group of symptoms most commonly described under this title resembles scabies.

Symptoms.—The early lesions are pinhead sized papules which may be discrete or grouped. These soon develop into vesicles which later become pustules. The sites of election are the hands, particularly between the fingers, the wrists, elbows, trunk and lower limbs. The face is usually exempt. Castellani and Chalmers limit the term craw-craw to a symptom complex described by Plehn under the title dermatitis nodosa. This is a papular disorder with lesions usually limited to the legs and arms though at times all portions of the surface except the face and scalp may be involved. The papules are hard, irregular or round, flattened or acuminate from millet seed to pea-sized and sometimes capped with scales. Secondary lesions occur from scratching.

Etiology.—The disease is contagious. O'Neil isolated a small filaria-like parasite from the lesions which Manson suggested might be *Filaris perstans.*

Treatment.—Plehn used successfully a 3 per cent. solution of lysol. Boric acid solution, mercuric chlorid 1:2000 and salicylic acid preparations are also recommended.

Cimex Lectularius.—**Synonyms.**—Bed bugs. Acanthia lectularia. French: Punaise des Lits. German: Bettwanze.

Bed bugs attack the skin of children as well as of adults. The parasite resides in various articles of furniture, including chairs, sofas, beds, cushions of vehicles, as well as in the cracks and crevices of floors and walls of apartments occupied by people of all ages. Man is only a temporary host when the parasite is seeking food. The insect is an apterous member of the order *cimicidæ* and is of a rusty or reddish color, this varying with the amount of blood with which it is distended. It emits a peculiar odor which is more distinct when it is crushed. It is provided with a blunt, pointed head, broadly attached to the thorax; two long, slender antennæ; and a three-pointed haustellum capable of projection and retraction beneath the head. It has three pairs of long slender legs which enable it to make rapid movements. The abdomen is broad, flattened, and oval in shape, with nine segments. The lesions of the skin are the result of the bite of the insect. The characteristic lesion is a red wheal having a whitened center and a central purpuric spot. They may be few or numerous and in infants and children are frequently accompanied by secondary lesions due to scratching, vesicles, pustules, crusts, purpuric blotches and infiltration. The parts of the body most frequently attacked are the ankles, legs, about the buttocks, neck and shoulders.

Diagnosis.—The lesions produced by bed bugs are to be distinguished chiefly from urticarial lesions induced by other causes. The location of the lesions and the peculiar hemorrhagic spot in the center of a reddened wheal with a white center is diagnostic.

Treatment.—The cutaneous irritation may be relieved by applying one of the following formulæ:

℞.	Zinc oxid	15
	Amylum	15
	Glycerin	6
	Liquor calcis	120
	Aqua rosæ, q. s. ad	240
M.		
℞.	Liquor carbonis detergens	15
	Lotio nigra	120
	Oleum olivæ, q. s. ad	240
M.		

Prophylaxis includes thorough cleansing of the infested areas with soap and water, scrubbing and application of mercuric chlorid solutions, together with boiling of bed linen and all infested clothing.

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CLASS III. ARTIFICIAL DERMATOSES (KNOWN ETIOLOGY)

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Chicago, Ill.

Dermatitis Calorica.—Definition.—When the skin is exposed to marked extremes of temperature inflammation results which is given the general designation dermatitis calorica. If the temperature extreme is of heat the condition is called *dermatitis ambustionis;* if of cold, *dermatitis congelationis.*

Dermatitis Ambustionis.—Symptoms.—Clinically burns are considered to be of the first, second, or third degree. All three forms may be present in a given case, depending on the manner and intensity of the exposure. Burns of the first degree are characterized by simple erythema with slight swelling and some local pain and tenderness. In those of the second degree the erythema is attended with more pronounced swelling, vesicles and blebs are formed, and the subjective symptoms are more severe and persistent. In third degree burns the dermic tissues are actually destroyed to a varying depth according to the intensity and duration of the exposure; the skin affected becomes an escharotic mass and the symptoms and complications incident to the sloughing process are often severe and threatening. Pain and tenderness, which may be slight at first, later becomes severe and constant; shock may develop in the earlier stages; secondary infection is almost certain to occur; and as healing progresses symptoms of disturbance of internal organs may appear, particularly of the stomach (ulcer) and of the kidney (amyloid).

Pathology.—The pathology of burns is that usually found in inflammation arising from acute damage to the tissues. The various lesions which may be present—erythema, vesicles, bullæ, necrosis, ulceration—are all dependent upon the same process, and are expressions of the degree of reparative inflammatory reaction which has been made necessary by the damage to the skin.

Etiology.—Scalding by hot liquids and fire accidents are the most common causes of burns in children; the former with the very young, the latter with those older. In general the incidence is more frequent among the poor and ignorant classes since with these the potential danger to the child of coming in contact with hot things, which arises from his natural helplessness and undeveloped judgment, is accentuated by inadequacy of family resources, and by inefficiency or absence of parental supervision.

Prognosis.—In general the prognosis of burns in children is not as good as in adults. Those of the first degree usually clear up promptly; if extensive in area considerable constitutional disturbance may be present for several days. Those of the second degree heal more slowly; when uncomplicated there is no scar formation. Careless dressing of bullous lesions may delay healing by permitting infection and destroying new epithelial growth; and, when extensive, second degree burns may develop toxic symptoms of grave import. Third degree burns are always serious; if death from shock does not supervene the process of repair proceeds slowly; scar formation is inevitable and often deforming; skin-grafting may become necessary, and complications from infections and toxemia (acidosis) are constant possibilities.

Treatment.*—Burns that are merely erythematous need but little treatment beyond protective measures. A cold compress applied for a few hours will relieve local discomfort, after which a simple dusting powder may be used. In burns of the second degree the blebs should be evacuated with aseptic precautions by horizontal puncture through the periphery of the roof-wall at the level of the skin; gauze dressings may then be applied wetted with a 5 per cent. solution of sodium biborate or bicarbonate, or with a saturated solution of boric acid, or with a 0.1 to 0.2 per cent. solution of picric acid in water. Lotions of olive oil and lime-water are also useful. To conserve the newly forming epithelium in denuded areas it is well to apply beneath these dressings a cross-hatching of narrow sterile gutta-percha strips; this provides drainage and permits the removal of the dressings without damage to the new cells. In more severe burns symptoms of shock must be met with suitable stimulating and sustaining measures. If acidosis develops alkalies and carbohydrates (glucose) are indicated. On account of pain anodynes may be necessary, but these should always be used with caution with reference to both immediate and remote effects. Locally, applications which meet the indications for second degree burns may be used at first; later, when sloughs have separated, the treatment becomes that of skin ulceration. Other therapeutic measures are the so-called open-air treatment, the continuous water-bath, and the use of paraffin of low melting point sprayed upon the skin in a melted condition to form when solidified an impervious coating under which repair may take place with a minimum of interference. This latter method, though greatly lauded, is not well adapted for treating third degree or very painful burns.

Dermatitis Congelationis.—Definition, Symptoms, and Pathology.—The changes in the skin resulting from exposure to extreme cold are not greatly different from those produced by extreme heat. Because of this clinical similarity the same division of the lesions into three groups according to degree is followed. In the first the part affected presents a dusky hyperemia and is slightly swollen; in the second bullæ form within the area of congestion; while in the third the freezing is so intense as to lead to local necrosis of the skin tissue. For the production of the mildest form the exposure to frost must be brief in time. Very often a chronic passive hyperemia with more or less local discomfort is induced by repeated or prolonged exposure to low degrees of temperature, but not sufficiently low actually to freeze the skin; this condition is known as *pernio* (*q. v.*).

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* Rocher and Lassere, J. d. med. d. Bordeaux, li (1921), pp. 51–79 (treatment in infants).

Harrington and Boorston, Ann. Surg., Philadelphia, lxxii, pp. 616–624 (orthopedic treatment).

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In sharp contrast to that in burns the initial pain in congealation is slight, due to the fact that the previous exposure of the skin to cold has numbed the nerve terminations. The part frozen is cold to the touch, hard, sometimes brittle, pale or white in color, and more or less insensitive. Hyperemia, swelling, and pain appear after thawing has taken place. Bleb formation and the more serious condition of local necrosis dependent upon the intensity and duration of exposure become apparent later as the inflammatory reaction evolves. The pathologic changes in congealatio are not materially different from those of ambustio. In the milder forms the hyperemia is of the venous rather than arterial type. In the more severe conditions the evolution of the inflammatory reaction follows along usual lines.

Etiology.—While the tender skin of the child is as vulnerable to extreme cold as to extreme heat the accidents of freezing are far less frequent than those of burning. Frost-bites are practically dependent upon the weather, are possible only during a small portion of the year, and are warned against by the presence of a very low temperature; burns may happen at any time without warning. Children who are the victims of bad economic conditions, who are poorly housed and insufficiently clothed, are the most frequent sufferers. The parts usually affected are peripheral: The ears, nose, fingers, toes, hands and cheeks. A contributing factor is sometimes found in the constriction, and consequent interference with circulation, of badly fitting garments or shoes intended for protection against cold.*

Prognosis.—Frost-bites of the first and second degree are usually not extensive; their prognosis is good though complete restoration may be slow. Extensive and severe freezing of the skin is always serious; death may occur from shock or from the complications which may develop during the prolonged healing process.

Treatment.†—Whenever possible the frozen part should be thawed by friction with ice or snow; this will lessen pain and tissue damage. Thenceforth the treatment is essentially that of burns and should be determined by the degree of disturbance present. The chronic passive congestion which may follow very slight frost-bites is best treated by the use of stimulating lotions (*vide* article on "Pernio"). Severe freezing of the hands or feet may necessitate amputation.

Dermatitis Venenata.‡—**Definition.**—The inflammatory reaction produced by skin contact with chemical substances is known as dermatitis venenata.

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* Dopter and Temoin, Bull. Acad. d. med. d. Par., 3 s., lxxxii (1919), p. 95.

† Von Eiselsberg, Munchen. med. Wchnschr., lxiii (1917), p. 871; and Smith and others, N. Y. Med. Jour., cvii (1918), pp. 23–25.

‡ For general discussion of this subject see the monograph on "Dermatitis venenata" by James C. White, Boston (1897); and paper by same writer in J. Cutan. Dis., xxi (1903), p. 441.

Etiology.—The number of substances, animal, vegetable, and mineral, capable of irritating the skin is very large, and opportunities for contact with them are very frequent. In general, exposure usually occurs through the medium of the clothing; in the trades and the various manual activities of life; through the external application of medicaments; and by accident. The skin of the child, more delicate than the adult's, reacts more readily to irritants. Children under 12 are seldom if ever exposed to the possibility of a trade eruption; and irritation from the application of medicinal substances is relatively infrequent. The effect of the retention of irritating material in contact with the skin by the clothing is well illustrated in the so-called diaper erythema of Jacquet; and the bright-red scaling cheeks of the over-washed child in winter show the effect of the excessive use of soap and water. Older children are often the accidental victims of irritating contacts with plants in house or garden or in places frequented by them in play.

The number of plants capable of irritating the skin is large. While certain well-known sorts are the usual offenders it is probable that many cases of dermatitis of obscure origin in out-of-door children are caused by unsuspected weeds and flowers. Among the common varieties of these the following have been credited with irritating qualities: Mayweed, burdock, mullein, mandrake, goldenrod, ox-eyed daisy, jack-in-the-pulpit, wood-anemone, larkspur, nasturtium, geranium, and tomato. The so-called "poison-ivy" is widely distributed in the United States. In settled districts it is a constant source of danger to children especially in the smaller towns and villages where it is frequently found in abundance along the streets and paths, and in the vacant lots—places which children tend to seek for purposes of play. The irritating principle in the plant is chemically an acid; direct contact with it is necessary; the wet skin is more susceptible than the dry; mere proximity to the plant will not produce a dermatitis, though dew splashed from the plant and the smoke from the burning vine have been known to carry the irritant. The primrose,* second to poison-ivy as a producer of skin irritation, is usually found as a potted plant in the home, often in the sick-room as a flower gift; as such it is a source of danger to all in the home, though somewhat less to the children than to the adults.

Symptoms.—The symptoms resulting from irritating contacts are variable, ranging from a mild circumscribed erythema with slight subjective disturbance to an extensive erythematous, vesicular, or bullous inflammation with marked edema, and distressing sensations of itching, burning, and pain. While many cases of dermatitis venenata fall within the milder group and show little more than slight erythema, vesication, and skin discomfort, it is usual to consider the reaction produced by poison-ivy as representative of this dermatosis. Contact with this plant is followed in a few hours by redness and burning of the part involved; swelling quickly supervenes, edema develops, and vesicles and blebs make their appearance. The local sense of burning is soon augmented by a severe pruritus; finger contacts for the relief of this are followed by the spreading of lesions to other parts of the body. These new areas are usually circumscribed, but in some instances the dermatitis may become quite generalized. Children are particularly apt to spread their eruption by scratching. After several days the vesicles and blebs dry up; the swelling subsides; and desquamation sets in; the itching usually continues and may persist until after the skin becomes normal in appearance; in many cases pruritus must be considered the most distressing complication of the convalescence period. The reaction from primrose contact is similar but in the main considerably less severe.

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* Foerster, J. A. M. A., lv (1910), p. 642; Sharpe, ibid., lix (1912), p. 2148.

Prognosis.—Recovery is usual though in some instances slow. Susceptibility to the responsible irritant remains after recovery and is in fact increased by the attack, as is also the general susceptibility of the skin to other forms of irritation.

Treatment.—The first consideration in the treatment of dermatitis venenata is the discovery and removal of the cause, and in the search for this inquiry should always be made as to possible exposure to poison-ivy or primrose. In the case of ivy-poisoning if the contact occurred but a few hours previously, an attempt may be made to abort the threatened inflammation by lathering the parts involved thoroughly with strong (laundry) soap. Mild cases of the erythematous and non-vescicular type will usually heal under a protective ointment or paste containing 0.5 to 2 per cent. of salicylic acid. If vesicles and bullæ develop these should be evacuated and the inflamed areas treated with applications of alkaline lotions until the lesions become dry, after which ointment dressings are indicated. To combat itching carbolic acid is the most efficacious; it should be used in low percentages, and when added to alkaline lotions should always be combined with 5 to 10 c.c. of glycerin to favor its solution; further, phenolated lotions should never be applied as continuous wet dressings except with great caution lest necrosis of the skin result. To offset the too-drying effect of certain applications, such as those containing lime-water, olive oil should be brought in contact with the parts two or three times daily; likewise, oil and not water should be used for the daily removal of accumulations of exudate and medicaments from the inflamed areas. If vesicles or blebs become infected a 2 to 5 per cent. ammoniated mercury ointment is indicated; or wet dressings of boric acid may be used. Spread of poison-ivy dermatitis to distant parts can be controlled in some degree by sealing each new lesion as it appears, provided it be not more than 1 cm. in diameter, with flexible collodion. Some success in the immunization of individuals sensitized to poison-ivy has been achieved by the oral administration over a period of time of a tincture of the plant itself.*

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* Schamberg, J. A. M. A., lxxiii (1919), p. 1213; Strickler, J. Cutan. Dis., xxxvi (1918), p. 327.

Dermatitis Traumatica.—Technically dermatitis traumatica comprises all injuries to the skin produced mechanically, as by rubbing, scratching, scraping, bruising, or laceration; practically the use of the term is confined to the more superficial types of injury. It is most commonly seen in combination with other dermatoses; in some of these it may constitute the initial stage, as in the impetigo which develops on damaged areas of the skin; in others it is a secondary manifestation, as in scabies and pediculosis. In children localized friction from ill-fitting clothing, continued contact with harsh garments, and scratching with the finger nails are the common sources of this form of dermatitis. If the first be combined with the retention of secretions, which is often the case, the simple redness from rubbing may be converted into a pronounced exudative inflammation. The thin and tender skin of infants and young children may be irritated to erythema by undergarments of doubtfully smooth texture; the so-called "flannel rash" is essentially traumatic in origin. The free fiber-ends on the surface of the finest wool fabric may traumatize, and the softest fleece-lined cotton material may become very rough if poorly laundered. Scratching of the skin, with the finger nails as the means of trauma, is the most important causal factor in children as well as adults; it is prompted by itching and so becomes a complicating element in all pruritic dermatoses. The lesions produced are linear, tending to become diffuse; they are erythematous and urticarial when superficial; excoriated and marked with hemorrhagic puncta when deep; these denuded lesions favor lymphatic infection and lead to infiltration of the deeper skin structures. The condition which induced the scratching is not helped by the process; rather, itching is increased, and a vicious circle is established if the traumatization is not checked.

Irritation from clothing will promptly disappear with the removal of the cause and the use of a simple dusting powder. The prevention of scratching, very often difficult in adults, is a constant problem with children. All discoverable sources of pruritus must be removed; particular attention should be given to the fit and quality of undergarments, to the habit and method of body bathing, to the presence of parasites in hair or clothing, and to possible exposure to insect bites. Any underlying dermatosis should receive prompt and suitable treatment. For the itching itself anti-pruritics are indicated; these should be used with an understanding of their possible deleterious effects. In very young children measures to restrain arm movements and the use of fixed dressings may be necessary. Excoriations may be healed with a salicylated paste of 0.5 to 2 per cent. strength; superficial infections of scratch marks will yield to a 2 to 5 per cent. ammoniated mercury ointment.

Dermatitis Factitia.*—Dermatitis factitia is the name given to any form of eruption produced intentionally upon the skin by the patient himself; it is synonymous with "dermatitis artificialis" and "feigned eruption." The lesions are usually caused to appear by the application of some strong chemical or by trauma, and may vary in type from a simple erythema to an extensive and deep destruction of the skin structures. As self-injury of this sort involves more or less pain and presupposes a definite purpose to be attained it is obvious that feigned eruptions are seldom seen in children. The requisite physical courage and the capacity for originating a motive and for executing skillfully the deceit is scarcely to be looked for in the average child, though these qualities might be found in the precocious individual. Further, when observed in children feigned eruptions are not likely to have been produced by chemicals since opportunities for gaining possession of and becoming familiar with such agents rarely come to a child. On the other hand, the impulse to imitate, which is so strong in the early years of life, might prompt a child to traumatize his skin by scraping or rubbing with some readily accessible object,* in imitation of some previously experienced accidental traumatization; especially if such accident had been followed by an appreciable and appreciated increase of personal attention from his parents or caretakers. Children have been observed repeatedly as subjects of "trichotillomania"† and of "trichokyptomania,"‡ conditions in which there is present an uncontrollable desire, respectively, to pull out forcibly, or to break off, the hair, thus producing areas of variable size in which the hair is more or less completely removed, and which may be taken for a ringworm infection.

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* Ormsby, J. A. M. A., lxv (1915), p. 1622 (report of large number of cases, full discussion, and bibliography).

In the recognition of dermatitis factitia the sudden development of the lesions, their rapid attainment of acme, and their failure to conform to the usual in appearance, configuration, distribution, and evolution are points of great diagnostic importance. A careful consideration of the personality and environment of the patient may prove helpful. In any persistently puzzling dermatosis it is well to review the possibilities of its being a feigned eruption.

The prognosis, as regards the healing of the immediate lesions, is good under proper treatment. If the deeper structures of the skin have been damaged scarring will result. As regards recurrence the outlook is usually not good.

The applications used in treating feigned eruptions must be determined by the nature of the lesions present, since these may be erythematous, dry or moist, acutely inflammatory, ulcerative, or deeply necrotic. The dressing must be of a fixed type so that it cannot be removed by the patient. Because of the peculiar psychologic conditions which usually obtain in these cases, the greatest care and discretion must be observed by the physician in the management of the patient and the relatives if experiences of unpleasant nature are to be avoided.

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* Fournier, H., J. mal. cutan. et syph.

† Besnier, Monatsch. f. prakt. Dermat., Hamburg, ix (1889), p. 572.

‡ Sutton, J. A. M. A., lxvi (1916), p. 185.

Radiodermatitis and Radium Dermatitis.*—Radiodermatitis, produced by an excessive dosage of the Roentgen-ray, and that resulting from a similar use of radium are without essential difference, and the first term might properly be applied to both conditions.

Radiodermatitis is peculiar in that it develops gradually, is without initial pain, and is attended with fall of hair from the part affected. The amount of *x*-ray necessary for the production of a so-called burn is variable, dependent upon many factors; an important one of these is the degree of vulnerability of the skin. As with dermatitis calorica severity is indicated in degrees. A radiodermatitis of the first degree is characterized by erythema with slight swelling; it appears after a latent period of about two weeks; is attended with mild pruritus; and subsides with some transitory pigmentation and scaling, with minute telangiectases as a late result in some cases. In the second-degree type the latent period of about 10 days is followed by lividity and swelling of the part; bullæ quickly form, to be succeeded by excoriations with an abundant serous or purulent exudate. Considerable pain is present; healing is slow, and skin atrophy, pigmentary changes, alopecia, and telangiectases may be looked for as end results. In third-degree *x*-ray burns the latent period is still shorter, the inflammatory reaction is severe enough to produce rapid necrosis of the skin structures; pain is severe; and the healing of the ulcerations is prolonged over an extended period with the ultimate production of deforming scars, marked atrophy, pigmentary alterations and vascular dilatations.

The chronic form of radiodermatitis, with atrophy, pigmentations, telangiectases, and keratoses tending to malignancy, which is due to a more or less constant exposure to an attenuated *x*-ray, is not to be looked for in children, though it resembles very closely a condition occuring practically only in the young, namely, xeroderma pigmentosum.

The pathologic alterations of the skin under *x*-rays start with degenerative changes in the deeper layers of the epidermis, in the cells of the root-sheath of the hair, and in the intima of the blood-vessels. With more intense action the less highly differentiated cells are also involved.

The prognosis in mild reactions is good; the skin functions are practically unchanged, though the possible slight telangiectases may be considered by some a disfigurement. In the burns of the second degree the appearance and function of the skin of the area affected may be considerably altered without, however, interfering with the patient's health or efficiency. Third-degree burns are unfavorable in that to the disfigurement and function impairment is added the possibility of malignant change in the scar tissue. In general the dangers to the patient and physician attending the use of *x*-ray and radium with children are greater than with adults; first, because the skin of a child is more vulnerable, and second, because his legal status as a minor makes it difficult for the physician to protect himself against possible medico-legal complications should the results of radio treatment be unsatisfactory. These factors entail on the pediatrician the need of care and caution in the use of these therapeutic agencies. This is particularly true in the treatment of fungus infections of the scalp, since in all instances a fall of the hair is involved, and in the case of favus a permanent alopecia is practically certain to result which is independent of any effect of the *x*-ray but which might be attributed by parents to incompetency in its use, with unpleasant results to the physician.

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* For a full discussion of all phases of this subject see MacKee's "*X*-rays and radium treatment, diseases of the skin," ch. xv–xvii, Philadelphia (1921).

As a preventive of complications in every instance the technique of applicaion of *x*-ray or radium for the condition under treatment should be understood and correctly followed, and the parents or guardian should be informed as to the nature of the agent used and the results that should be expected. If a fall of hair is looked for, or the actual destruction of tissue is sought, those concerned should be so told. The treatment of such inflammatory reactions as follow must be expectant. In general the management of *x*-ray burns does not differ materially from those produced by extremes of heat. Healing in the severe forms may be very slow due to trophoneurotic changes which do not occur in dermatitis calorica; and the use of measures which will stimulate the restoration of tissues and will protect the new growth of cells may have to be followed up with particular patience and perseverance.

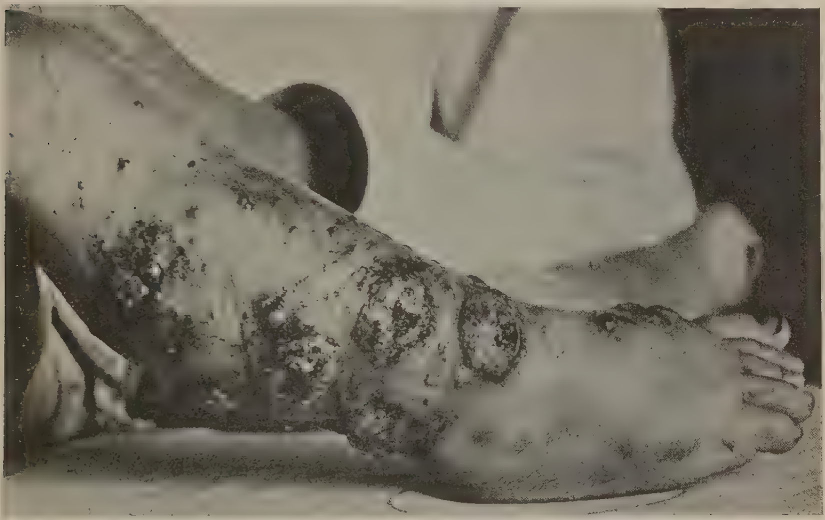

FIG. 35.—Bromide eruption (from cough medicine). (Fordyce and MacKee.)

Dermatitis Medicamentosa.*—**Definition.**—Dermatitis medicamentosa is the name given to those eruptions of the skin which result from the systemic absorption of drugs, whatever may be the route by which the latter are introduced into the body.

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* Morrow, "Drug eruptions" (with notes by Colcott Fox), monograph Sydenham Society (1893); Stowers, Brit. J. Dermat., London (1898), p. 289; Hartzell, Boston Med. and Surg. J., clxxx (1919), p. 163.

Symptoms.—Medicinal rashes may be attended with few subjective symptoms, but usually itching and skin discomfort are fairly marked. Constitutional symptoms may be somewhat complex since they may comprise those for which the medicament was given plus those representing the physiologic or toxic action of the drug. The rash usually appears suddenly and is most frequently erythematous or morbilliform in type, with a tendency to disappear promptly under suitable therapy. Certain drug eruptions however, notably those produced by the iodids and bromids, evolve more slowly, are more resistant to treatment, and are more markedly inflammatory in type, the lesions being pustular, carbuncular, ulcerative, vegetative, or verrucous, often followed by scarring, and always attended with greater local discomfort.

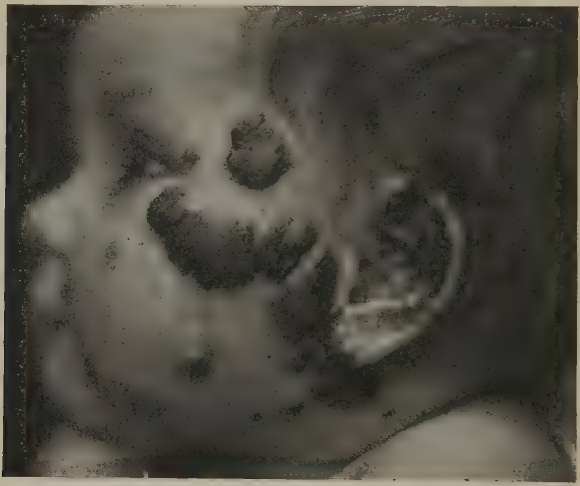

Fig. 36.—Bromide eruption. (Collection of Dr. Grover W. Wende.)

Etiology.—The list of drugs capable of producing skin rashes through systemic action is very large. While the lesions are usually of the types named above cases representing other of the primary and consecutive forms have been recorded. More than one type of lesion may appear from a drug in a given case. Susceptibility varies with individuals; poor health and insufficient elimination are considered predisposing factors. Various theories have been put forward to explain drug-rash susceptibility; of these that of anaphylactic action* and that of toxic action, either local or systemic, are most in favor; the true cause, however, is not yet positively known. Children are rather more prone to these eruptions than adults, but this may be due to the fact that with them the maximum dosage is more frequently exceeded. But as the number of drugs ordinarily used with children is not large the incidence of dermatitis medicamentosa in childhood is rather less than in the later years of life. Children at the breast may show on their skins eruptions due to medicaments ingested by their mothers. If a child is susceptible to a drug one or a few doses suffice to produce the rash; if his level of tolerance is high a more or less prolonged administration is necessary. The eruption may appear after the drug has been withdrawn; and it may persist for some time after the intake has ceased, though usually it disappears promptly with the removal of the cause.

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*Straus, Therep. Monatsh., Berlin, xxxii (1918), pp. 460–162.

The following is a list of drugs in common use among children, with the form of eruption usually produced by them:

Aconite—vesicular, with considerable itching.
Arsenic—erythematous, pigmentary, hyperkeratosis.
Arsphenamin—erythematous, urticarial, generalized dermatitis.
Belladonna*—scarletiniform erythema.
Bromides†—acneiform, inflammatory nodules and plaques, with pustulation; may simulate the granulomata.
Iodids‡—types multiform, any lesion may be possible; most often pustular.
Opium—erythematous.
Quinin§—scarletiniform erythema.
Santonin||—urticarial.

Diagnosis.—The sudden and unlooked-for appearance of a more or less generalized eruption in a child who is taking medicine or who is being nursed by a mother under medication should suggest the medicament as causative. Absence of those systemic symptoms which attend the various exanthemata is an important point. A careful consideration of the factors in the case will exclude easily some of the commoner skin irritations of children such as prickly heat, intertrigo, diaper rash, insect bites, lichen urticatus, etc. Greater difficulty would arise in those instances in which an erythema-producing drug, such as belladonna, has been given to combat symptoms similar to those of the pre-exanthem stage of scarlet fever or measles; an immediate diagnosis may not be possible in such a case. The iodids or bromids taken by mothers for syphilis or epilepsy should always be remembered a source of unusual eruptions in nurslings.

Prognosis.—The ordinary erythematous, morbilliform, or urticarial drug rash clears promptly under suitable therapeutic measures. The more severe types with bullous, vegetative or ulcerative lesions such as may follow the iodids or bromids are much slower to disappear and may require prolonged local treatment; scar formation may be

* Knowles, Am. J. Med. Sci., Philadelphia (July, 1911).

† Jackson, J. Cutan. Dis. (1895), p. 462; Knowles, New York Med. J. (Mar. 20, 1909).

‡ Hyde, J. Cutan. Dis., iv (1886), p. 383; Montgomery, D. W., Tr. Med. Soc., California (1900).

§ Stelwagen, J. Cutan. Dis. (1902), p. 13; Meltzer, Munchen. med. Wchnschr., lxv (1918), p. 20.

|| Sieveking, Brit. Med. J. (Feb. 18, 1871).

looked for. Susceptibility to the causative drug remains after the eruption disappears; the bearing of this fact on the question of future attacks is obvious.

Treatment.—In all cases withdrawal of the drug is the first indication; if a nursing mother is the source and the medication must be continued weaning of the child becomes necessary. Attention should be given to elimination. Locally, for the milder forms, a dusting powder or an alkaline antipruritic lotion occasionally applied is all that is needed. For the severer types with pustular, carbuncular, vegetative or ulcerative lesions, the local treatment must be adopted to the indications present.

Serum Eruption.*—The subcutaneous administration of antitoxic or other sera is frequently followed by the so-called "serum eruption." This exanthem, together with certain more or less constant systemic symptoms such as fever, general malaise, joint pains, respiratory embarrassment, etc., constitutes what is known as "serum sickness." The eruption is usually urticarial, but may be erythematous, of scarletiniform or morbilliform type; localized or generalized edema is a common accompaniment. The underlying pathologic process is essentially anaphylactic, arising from the introduction into the system of a foreign serum. In the evolution of the eruption and the attendant symptoms some differences are observed, dependent upon the number and relationship of the doses given. When a patient receives an injection for the first time there is no skin reaction at the site of entry, but some fever and malaise may develop within the first 24 hours. After an incubation period of 8 to 12 days the eruption may appear; this attains an acme in one to three days and gradually fades. This evolution of symptoms following the initial injection, in the order and time given, has been designated the "normal-time reaction." Sensitization to the serum given is established in about 10 days. When a re-injection is made after sensitization a sharp edema develops at the point of entry within a few hours or at most 24, attended with slight systemic symptoms; this total response is known as the "immediate reaction" and subsides rapidly. It is followed in from six to nine days by a rash and general symptoms; these may be quite severe. This second disturbance, having a shorter incubation period than the "normal-time" reaction, is known as the "accelerated reaction." If re-injection is done before sensitization has developed there is no immediate reaction and the second reaction remains normal-time. Sensitization is quantitatively influenced by the amount of serum first injected and may persist for years.

Antitoxic sera have been so perfected in recent years that the liability to serum disease is now greatly reduced. To avoid possible trouble when antitoxin must be given the initial dose should be of sufficient therapeutic strength to accomplish the result desired, and if re-injection becomes necessary it should follow within a week of the initial dose if possible. Inquiry should always be made as to whether the patient has ever before received serum treatment. As a preventive of anaphylactic shock it has been recommended that atropin, in a dosage approaching the maximum for the individual, be administered hypodermically about one-half hour before the serum is injected.

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* For a full consideration of this subject with extensive bibliography see monograph by von Pirquet on "Allergie." Berlin (1910), also; Kolmer, Infection, Immunity, and Biologic Therapy, Phila., 1923 (chapter on Allergy).

For the eruption itself anti-pruritic lotions may be used if the itching is annoying; otherwise a simple dusting powder is sufficient. Attention should be given to the elimination.

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CLASS IV. SKIN DISEASES OF UNKNOWN ETIOLOGY

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Erythema Hyperemicum (**Erythema Simplex; Erythema Congestivum**).—Hyperemic erythema is a disorder distinct from exudative erythema, and is characterized by diffuse, non-elevated, pink or rose-red patches of variable size, which disappear temporarily upon pressure. The term should be confined to the varieties which are systemic in origin and should exclude those produced by external agents which cause a dermatitis.

Erythema hyperemicum is an expression in the skin of numerous physiologic and pathologic causes operating through the central or peripheral vasomotor mechanism. It is frequent in children, probably owing to their nervous instability. Toxic products of systemic febrile diseases and of digestive disorders are frequent causes, and it may follow vaccination, the injection of sera, and the ingestion of certain drugs.

Redness, which disappears upon pressure, occurring in patches of variable size or in small spots or macules, is the essential symptom. The erythema may be more or less general, often symmetrical, appearing over large areas in patches or as a continuous sheet of redness, or it may be present in discrete or closely crowded spots and resemble an exanthem. Infiltration and elevation are absent, though an urticarial tendency is observed at times. Involvement of the mucous membranes is infrequent. The eruption is usually transitory, and disappears within a few days, with little or no desquamation. The generalized rashes due to gastro-intestinal disorders may be accompanied by slight febrile action.

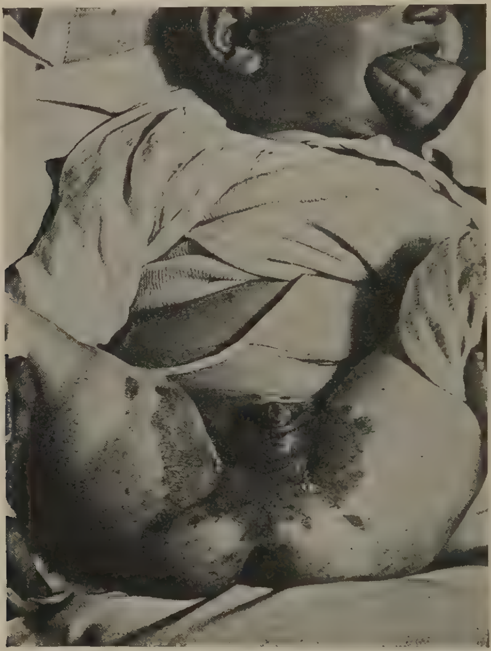

Fig. 37.—Diaper eruption. (Fordyce and Mackee.)

Roseola infantilis is a term applied to the more generalized types of hyperemic erythema appearing as macules or fine papules, most common on the trunk, and accompanied by fever and systemic disturbance. It may closely simulate measles, rubella, or scarlet fever.

Diagnosis.—The diagnosis of hyperemic erythema is ordinarily readily made by the absence of the characteristic features of the eruption and the other accompanying symptoms of the acute exanthemata, and by the determination of the internal cause.

Treatment.—Internal treatment is directed toward removal of the cause. If the disorder is digestive in origin gray powder or fractional doses of calomel are of value. Local treatment, other than with simple dusting powders, is seldom required. Calamine lotion with the addition of glycerin, or a weak carbolic acid lotion, 0.5 to 1 per cent. strength with witchhazel, may be employed.

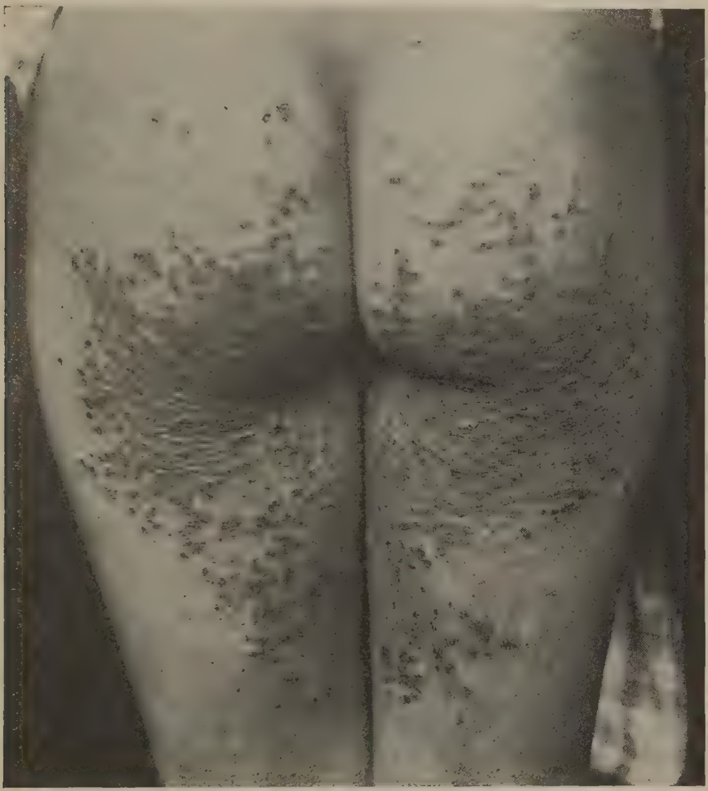

FIG. 38.—Erythema of Jacquet. Erythemato-papular form. Seven years' duration. Complete disappearance after *x*-ray treatment. (Collection of Dr. Grover W. Wende.)

Napkin Erythema (Erythema of Jacquet).—Definition.—This is an eruption which occurs on the convex surfaces of the napkin region of infants, characterized by deep-red and shining erythematous patches, with the later consecutive development of vesicles, erosive papules, and small ulcerations.

The condition was first clearly defined by Jacquet[1] and its importance has recently again been emphasized by Adamson[2] whose articles form the basis for the following description.

Symptoms.—The eruption occurs in infants upon the prominent convex surfaces of the area covered by the napkin or diaper, which includes the convexities of the lower abdomen, external genitals, perineum, upper and lower halves of the thigh, buttocks and scrotum, and also the calves and heels which come into contact with the napkin when the legs are flexed. In the beginning the eruption is essentially a patchy erythema, deep red and glazed, with smooth surface, tending to exudation, and limited to the convex areas. This type is seen most often in very young infants. In a later stage the development of small vesicles within the patches and of small, red, disc-like erosions is observed, which may coalesce and thus form polycyclic lesions.

The formation of flattened granulations on the base of the erosions causes these to assume the character of papules (erythemato-papular, or post-erosive type of Jacquet) and it is this stage which gives importance to the disorder, because of the resemblance of its lesions to those of congenital syphilis. Adamson says: "The eruption occurs like the preceding type over the prominent parts of the convex surfaces. The lesions consist of flat, bright-red or dull-red papules, or pseudo-papules, arranged in groups, which may or may not be set upon an erythematous base. These groups of pseudo-papules are seen upon the buttocks, the upper half of the thigh, the lower half, the calf, and on the genitals. They are never found in the flexures or sulci dividing the convex areas. They may be associated with erythema of the heels and of the lower abdomen." This type is most frequent in infants several months old.

Instead of granulating the erosions may become transformed into punched-out, shallow or deep, more or less circular ulcers, which by confluence form polycyclic defects. The convexities of the scrotum and adjacent parts of the buttocks and thighs are the usual areas affected by the ulcerative type, which rarely involves the sulci or flexures. Though described as occurring in consecutive stages, there is no sharp definition of the process, and its different lesions co-exist not infrequently.

Etiology and Pathology.—The histopathology of these lesions has been studied by Ferrand[3] who found spongioid transformation of the prickle-cell layer and vesication in the earlier stages, closely resembling the changes observed in eczema. In the later types the changes consist chiefly of hyperacanthosis, parakeratosis, cell infiltration of the papillæ and derma, with occasional spongioid change. Conclusive bacteriologic studies are lacking, though the character of the lesions is suggestive of a streptococcic origin.

The characteristic distribution indicates that local irritation from wet or soiled napkins is an important etiologic factor. In a series of cases observed in the Milwaukee Infants' Hospital the condition was definitely attributable to an excess of soap remaining in the napkins after laundering and sun-drying. The severe types are most often encountered in conditions of malnutrition; in many cases there is no discoverable gastro-intestinal disorder.

Diagnosis.—The lesions observed in the erythema of Jacquet closely simulate the polymorphous syphilitic eruptions of the newborn. The characteristic limitation of the lesions in Jacquet's erythema, the non-involvement of face, palms and soles, the red rather than coppery hue, and the absence of definite symptoms of congenital syphilis such as hoarse cry, snuffles, and fissures of the lips and at the angles of the mouth, the absence of the spirochete from the lesions, and a negative Wassermann reaction in child and mother, all serve to differentiate this disorder from syphilis. As long as the diagnosis is in doubt every precautionary measure must be taken to avoid contagion.

Seborrhoic dermatitis as seen in infancy at times invades the napkin area as a rapidly developing, diffuse inflammatory eruption, for the most part covered with small, granular, greasy, yellowish scales, and with a smooth and satiny, deep-red surface in the prominent parts. In the folds of the skin the eruption is often moist or exudative. The margins are fairly well defined, and beyond them many tiny, discrete, scaly papules and often small patches will be found. The eruption in the napkin region is only part of a widespread disorder, which has its origin on the scalp and extends from it to affect especially the folds behind the ears, the naso-labial region, forehead, sides of the neck, axillæ and umbilicus. The favorable response to treatment with weak sulphur ointment is suggestive of a local microbic origin of this disorder.

The diagnosis from the erythema of Jacquet is based on its essentially small papular character, the presence of characteristic greasy or moist, yellowish, granular scales, fairly definite margin, coincident involvement of the scalp, retro-auricular folds and other areas, and the absence of erosions and ulcers. These features also serve to differentiate seborrhoic dermatitis in this location from the lesions of congenital syphilis, emphasized by the absence of snuffles, oral fissures, lesions on the palms and soles, and other signs of syphilis.

Eczema occurs only rarely on the buttocks of an infant, and affects essentially the forehead, cheeks and scalp, as an intensely pruritic, vesicular, weeping eruption, often covered with gummy crusts.

Treatment.—In the management of the erythema of Jacquet scrupulous cleanliness is of prime importance. The diapers should be changed frequently to avoid maceration of the epidermis, especially if an impervious material is used as an outer covering. The diapers should be thoroughly washed, without an excess of soap, well rinsed, and sun-dried if possible. The parts are to be sponged freely with warm water without the use of soap, or with boric acid solution. In the earlier erythematous or erosive stages zinc oxid-calamine emulsion is of value, followed by a simple dusting powder. If oily preparations are not well tolerated the zinc-calamine lotion may be used instead. Crusts are to be removed by bathing with boric acid solution after which a borated zinc-talc powder is applied. When ulcers are present they are to be cleansed carefully and then covered with a 2 per cent. ammoniated mercury ointment. If the latter is irritant to the skin, diluted black wash (lotio nigra) may be substituted. The disorder usually responds readily to this treatment. Infants with intestinal disorders or in a state of malnutrition require treatment directed to these conditions.

Erythema Intertrigo (Eczema Intertrigo; Chafing).—Definition.—Erythema intertrigo as observed in children is a hyperemic condition which occurs in the folds of opposing cutaneous surfaces, and is induced by heat, moisture, and friction.

Symptoms.—The localities affected are the folds of the neck, the axillæ, the groins, the gluteal folds, the flexures of the larger joints, the scroto-femoral and the labio-femoral clefts, and the sulci between the upper and lower halves of the thighs. Intertrigo is frequent in fat children, and involves especially the inguinal folds and the anal and genital regions. The skin becomes hyperemic, its surface is macerated by the retained and altered perspiration, and superficial abrasions may develop, with a mucoid discharge. A single linear, superficial fissure of variable width is frequently formed in the depth of the larger folds. The disorder may not advance beyond this stage, but if neglected, or persistent, or improperly treated, an active dermatitis may develop with the formation of vesicles and an exuding, red surface. In persistent cases, especially in poorly nourished infants, superficial dermic abscesses or boils may develop as the result of secondary infection.

Etiology.—The causes are chiefly local. Friction and moisture initiate the disorder, which is further aggravated by prolonged contact of wet or soiled napkins. Irritant soaps and too vigorous attempts at cleanliness may also be factors in its production.

Diagnosis.—The disorder is readily differentiated from the erythema of Jacquet, which affects the convexities of the napkin area, whereas intertrigo appears in the sulci or folds of the skin and does not develop erosions or ulcers. The diagnosis from congenital syphilis is based on the superficial character of the erythema, the absence of infiltration, the vivid red color, and the usual presence in congenital syphilis of characteristic lesions upon other parts, and of other symptoms of that disease. Seborrhoic dermatitis when appearing in the localities also affected by intertrigo is recognized by the diffuse, inflammatory character of the eruption, its granular, greasy, yellowish scales, the outlying discrete or aggregated scaly papules, and by its forming in these localities only part of a general eruption. The occurrence, though rare, of diphtheria of the skin superimposed on an intertrigo must be considered when the intertrigo does not respond to treatment and assumes an erysipelatous hue, becomes densely infiltrated, and develops punched out ulcerations of irregular contour with a necrotic base, edema of the surrounding tissue, and accompanying constitutional symptoms.[4]

Treatment.—Cleanliness is an essential part of treatment, but the free use of soap and water should be interdicted. The parts affected are to be kept clean by washing with boric acid solution, carefully dried with absorbent cotton, and then covered with a dusting powder, such as that prepared according to the formula of McCall Anderson:

℞.	Pulv. zinci oxidi	oz. ½ (16)
	Pulv. camphoræ	dr. 1½ (6)
	Pulv. amyli	oz. 1 (32)

Various powders, such as boric acid, talcum, stearate of zinc, chalk, and magnesium carbonate may be used separately or in combination; a useful formula is:

R.	Pulv. acidi borici	dr. 1 (4)
	Pulv. zinci stearati	dr. 2 (8)
	Pulv. talci	oz. 1 (32)

To prevent friction the folds of the skin are to be kept from contact by the insertion of absorbent cotton or of several layers of soft gauze, which require frequent changing.

If exudation is present, mildly astringent lotions are often more effective, such as the zinc-calamine lotion, prepared as follows:

℞	Pulv. calaminæ	dr. 1½ (6)
	Pulv. zinci oxidi	dr. 1½ (6)
	Aq. calcis	oz. 1½ (48)
	Sol. acidi borici (3 per cent.), q.s. ad	oz. 6 (192)

Other suitable lotions are 1 or 2 per cent. solutions of subacetate of lead or of aluminum acetate, diluted with boric acid solution. Lotions are to be applied either by thoroughly dabbing on the parts from six to eight times a day, or on gauze as compresses for one-half hour, followed by dabbing liberally.

Ointments are usually not well tolerated in the folds of the skin, although emulsions may prove serviceable. A useful emulsion is one composed of equal parts of olive oil and lime-water, to which zinc oxid and calamine powder may be added.

Erythema Pernio (Chilblains).—Erythema pernio is a disorder of frequent occurrence in children during cold weather. It is characterized by the presence of persistent erythematous swellings on the hands, feet, ears and nose. The lesions occur as small oval, dusky-red to bluish, tense and glazed swellings, with the center darker or lighter in color than the border, or as larger patches of indefinite outline. They are cold to the touch, firm, and at times moist with perspiration. The accompanying characteristic itching and burning sensation is aggravated by exposure to warmth. In extreme cases the lesions are purplish in color, and vesicles, bullæ, and ulcers develop, with later scar formation. The lesions are single or multiple, at times bilateral, and may be symmetrical. They affect the ulnar border of the hands, the fingers, toes, heels, ears, nose, and less often the cheeks. The writer has seen a number of young children in whom, after exposure to cold, the disorder occurred in the lower portion of the cheeks above the line of the jaws, and beneath the chin, as firm, dusky-red, elongated, spindle-shaped, nodular swellings, as the result of constriction by tightly drawn cap ribbons.

The condition may be transitory, or may remain for weeks. When untreated it usually continues with exacerbations throughout the winter. It is especially frequent in children between the ages of 5 and 15 years, and is more common in females than in males.

Etiology.—The exciting cause is exposure to damp cold, in individuals predisposed by reason of a feeble peripheral circulation, resulting from anemia, vascular hypotension, and the so-called lymphatic constitution, and is favored by constricting articles of clothing. Wright believes that the coagulability of the blood is defective. It is a vasomotor disturbance, and due to inability of the vasomotor mechanism to maintain the normal vascular tone in the parts.

The frequently observed occurrence of erythema pernio in association with the scrofulous diathesis and with adenopathies has led some writers to classify the disorder as a manifestation of attenuated tuberculosis or tuberculide, a view which the writer does not share.

Diagnosis.—The diagnosis is readily made, except in persistent cases with scarring and atrophy, which may simulate lupus erythematosus closely; in fact, the two conditions may co-exist in the same patient. The "chilblain circulation" is common to both disorders, but the lesions of lupus erythematosus are usually slowly progressive, flat and not raised, show central atrophy and slight marginal infiltration, and rarely develop necrosis.

The lesions of papulo-necrotic tuberculide appear usually in the spring and autumn months, as small, often numerous, bright-red papules which tend to become vesicular, crusted, and necrotic in the center, and leave depressed pit-like scars.

Treatment.—Treatment should be directed to improvement of the circulation and general health. Protection of the affected parts by warmer covering, and active exercise or massage may be useful in preventing recurrence. Wright recommends the internal use of calcium chlorid, and some consider Fowler's solution in small doses of value as a preventative when given at the beginning of cold weather. The writer is not convinced of the value of either remedy, and places more reliance on maintenance of the general nutrition and on active exercise or massage. Local treatment requires the use of sedative and astringent applications, among the most useful of which is the lead-water and laudanum mixture, applied as a wet compress. When the condition in less acute brisk friction is indicated, followed by the use of camphorated soap liniment, spirits of bay rum, or other alcoholic lotions. Ichthyol in 50 per cent. aqueous solution, painted on the parts, or applied as a compress in 5 to 10 per cent. solution with 5 per cent. glycerin, is often effective, or it may be used in ointment in 10 per cent. strength. When vesicles or ulcerations are present, treatment with weak antiseptic wet dressings or ointments is required, and when the dermatitis has subsided, astringents may be employed. In sluggish cases balsam of Peru 12 per cent. and silver nitrate 1 per cent. in petrolatum is of value.

Erythema Scarlatiniforme or Scarlatinoides.—Definition.— The term erythema scarlatiniforme is applied to an eruption of varying etiology, closely simulating that of true scarlet fever, and followed by desquamation.

Ormsby recognizes two types: The acute, which is secondary to other infectious diseases, to auto-toxemia, or to food or medicinal toxemia, and the subacute type which may be idiopathic, secondary to other infectious diseases, or produced artificially by drugs.

Symptoms.—The condition develops suddenly, with or without a short period of mild prodromes (gastric, nervous and febrile) as a rapidly spreading exanthem, which may begin on any portion of the body, and reaches it full development within a few hours, or in two or three days at most. The eruption is usually universal, though at times the face may remain clear and the large joints may be only slightly involved, or the eruption may be limited in its extent. The eruption is either punctiform or macular, soon becoming diffuse and uniform, and the color may vary from bright to livid red, but is usually bright scarlet. Edema is often present, localized to the face, and miliary vesicles may develop. The mucosæ of the mouth and throat may be reddened, but the tonsils are not swollen and there is usually no complaint of sore throat. The tongue is coated, and later reddened, and very rarely is of the "strawberry" type. The accompanying general symptoms are usually mild, but may be severe, depending upon the particular cause. Fever is rarely high, and the pulse rate is never disproportionally high, as in scarlet fever. The eruption usually subsides after three or four days, varying according to its intensity. Desquamation often begins before the eruption disappears, but most often begins after three days and is completed in from two to three weeks. In exceptional cases the nails and hair may be shed. Desquamation occurs either in the form of small branny scales or in large, thin sheets, and varies on different parts of the body; occasionally an epidermal cast of the hands and feet is exfoliated almost intact. Lamellar desquamation is often followed by a branny type of scaling lasting for several days. Recurrences at intervals of one or many months are common, and should be distinguished from relapses, or a series of attacks separated by days only.[5]

The subacute form, or recurrent desquamative scarlatiniform erythema, described especially by French writers, is of longer duration, the erythema is more often intense and universal, constitutional symptoms are pronounced, and desquamation is profuse. Recurrences and relapses are frequent and the disorder may be practically continuous and closely resemble the primary erythrodermias.

Etiology.—Individual predisposition is a most important underlying factor in the etiology, the exciting causes being most often toxemic or septic, and at times external. Erythemas of this character may precede the eruption of varicella and measles, or occur in the course of diphtheria, rheumatism, small-pox, malaria, septicemic conditions, and follow the useof sera and the ingestion of various drugs and articles of food. External irritation from the use of mercury and iodoform may produce the disorder in typical form including recurrences.

Diagnosis.—The differentiation of scarlatiniform erythema from scarlet fever may be attended by considerable difficulty, especially in the early stage. As a rule, in scarlatiniform erythema the systemic symptoms are mild in character, angina is absent, the eruption is out of all proportion to the amount of systemic disturbance, the eruption appears rapidly and is often not generalized, desquamation begins early, leukocytosis is absent, there is no history of contagion, and not infrequently a history of previous attacks is obtained. If the diagnosis cannot be made, the case should be isolated; observation for one or two days will usually clear up any doubt remaining. The eruption when first presenting occasionally bears some resemblance to that of measles, but soon becomes diffuse, rarely begins on the face and often avoids it entirely, and in addition is not attended by the peculiar associated symptoms of measles.

Erythema scarlatiniforme is distinguished from the exanthem of rubella, or rötheln, which occasionally is of scarlatiniform type, by the absence of papules, some of which are always to be found in rubella, and by the absence of glandular enlargement.

Prognosis.—An attack usually runs its course within from 10 days to three weeks, and the general health of the patient remains unaffected. Relapses are frequent, however, and may prolong the course of the disorder to six or eight weeks. After a long interval of freedom a second attack may develop, and such recurrences may be repeated thereafter at varying intervals. If the cause of the erythema is a severe septic process or systemic disease, the ultimate prognosis is, of course, determined by the character of the underlying malady.

Treatment.—Systemic treatment is directed toward the elimination of the cause which has produced the erythema, if this is ascertainable. However, of necessity, treatment must often be based upon general principles. Free elimination should be secured. Salol or sodium salicylate, are advocated in moderate doses, and in the persistently exfoliating types quinin in full doses has been of service. The patient is to be confined to bed and kept warm, and guarded against chilling, while local applications are made. These should preferably be simple dusting powders, liberally applied, such as talcum or stearate of zinc, and if tension or stiffness is pronounced the skin may be anointed with a bland soft ointment, such as cold cream or boric acid (3 per cent.) in vaselin. During the stage of erythema ointments may prove irritating. Warm colloid baths, of oatmeal, bran or starch, followed by an emollient ointment, often relieve the feeling of tension and make the patient comfortable.

Erythema Multiforme.—Erythema multiforme is an acute inflammatory disease, often attended by mild systemic disturbance, and characterized by an eruption or red or bluish-red macules, papules and tubercles, or vesicles and bullæ, one type of lesion usually predominating. The eruption is often bilateral and symmetrical in distribution, and shows a marked predilection for the face, neck, and the dorsal surfaces of the the extremities below the knees and elbows. At times the eruption may be extensive and also involve the mucous membranes. The disease runs its course in from two to three weeks, and often recurs through a period of years in the spring and autumn months.

Erythema multiforme is not infrequently preceded or accompanied by malaise, mild febrile disturbances, sore throat, and rheumatoid pains in the larger joints. The eruption appears suddenly on the sites of predilection, as pinhead to fingernail-sized macules of pinkish color, which, within a few hours, become tumefied and papular, or enlarge into erythematous patches, with a distinctly bluish tint. During the first few days the lesions continue to enlarge and several fresh outbreaks may occur, followed by gradual subsidence of the disorder, or new lesions may appear for 5 to 10 days, with coalescence of older papules to form elevated, flat patches of bluish-pink or violaceous color.

The most common form of the disease is that in which papules predominate. These are usually discrete, pea-sized, flattened lesions, sometimes slightly depressed in the center, and as they enlarge some may become ring-shaped. In another form the eruption consists chiefly of erythematous patches varying considerably in shape and size. The ring form of lesion is frequently seen in this type of the disease (erythema circinatum or annulare), and when several rings coalesce by peripheral extension, with subsidence of the active process at the points of contact, gyrate or serpentine figures are formed (erythema figuratum or gyratum). In some instances more or less extensive patches of erythema spread at the border, which is well defined and

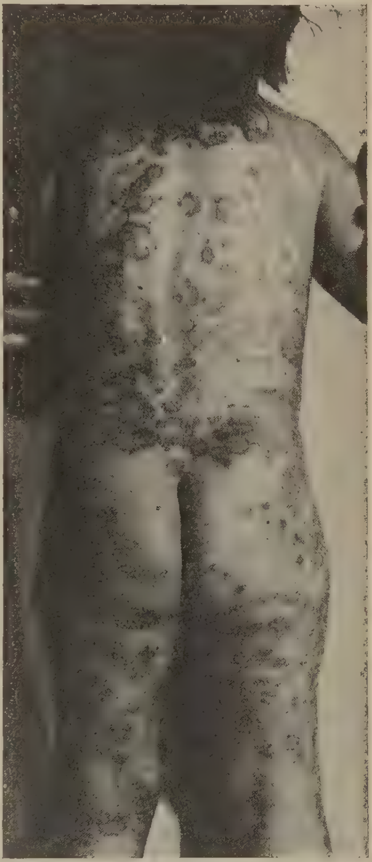

FIG. 39.—Erythema multiforme. (Fordyce and MacKee.)

slightly elevated, while the older central part subsides and fades to a chamois color (erythema marginatum). Occasionally the lesions have an opaline or urticarial appearance and itch intensely (erythema urticatum). In any of the forms of erythema multiforme, the inflammatory process may be of sufficient intensity in certain parts to produce vesicles and bullæ in addition to the usual eruption of papules and tubercles. In such cases involvement of the oral mucosa is not unusual, and exceptionally vesicles and bullæ develop on the lips and in the mouth before the skin is involved, or, rarely, may remain limited to the mucosa. Hemorrhage into the lesions may also take place, especially in the bullous form, attended by prostration, fever, and arthritic pains, with recurrences during several years.

In the variety designated as erythema iris, the lesions occur in varicolored concentric rings; the vesicular or vesico-bullous phase is known as herpes iris. It is most frequent on the dorsum of the hands and wrists, and at times is seen in the palms, and lower parts of the legs, on the face, and trunk. Similar, smaller lesions are also occasionally found on the lips and in the mouth, and in these cases the disease is apt to be recurrent.

The lesions in most cases are multiform, different types occurring simultaneously or successively, or changing from one type to another. The eruption may be limited in extent, or generalized and abundant, and include the mucous membranes of the eyes, mouth, and genitalia. The subjective symptoms are usually slight; burning and itching sensations are common, and at times the lesions are painful. Constitutional disturbances are generally mild in character, but may be severe at times, indicating an association with some infective process or visceral disorder. Osler has emphasized that the cutaneous symptoms may be manifestations of severe systemic disturbances of toxic or metabolic character with involvement of the gastro-intestinal tract, kidneys, brain, lungs, or joints.

Etiology.—Erythema multiforme occurs frequently in childhood, though more commonly in adolescence and early adult life. Its cause has not been established, but low-grade infections are probably the most frequent etiologic factor, especially in the "idiopathic" papular type of limited distribution. The frequent association with mild arthritic symptoms would point to such origin. It may follow the ingestion of certain drugs, of stale articles of food, and the use of antitoxic sera, and it occurs in connection with vaccination, accidental microbic infection (as in Corlett's case[6]) and visceral disease. The eruption which appears in response to the last named causes often differs from that seen in the "idiopathic" type, in that the lesions are not peculiarly localized and are not disc-like round patches with purplish center and spreading periphery.

The disease is an inflammatory process, the character of the lesions being determined by variations in the amount of exudation. According to the type of lesion examined, hyperemia is present due to vascular dilatation, cell effusion into the corium and subcutaneous tissue, slight rete proliferation, and a varying amount of transudation of serum resulting in the formation of edema, vesicles and blebs.

Diagnosis.—The diagnosis of erythema multiforme is based on the symmetry of distribution of the lesions, the characteristic localization of the papular type especially to the extremities and face, the tendency to ring-shape, the bluish-red color, the edematous character and multiformity of the lesions, the relative absence of subjective symptoms, the frequent association of rheumatoid pains, and the mild character of the constitutional symptoms, and the history of recurrent attacks. It is differentiated from urticaria by the absence of wheals, the symmetry and greater persistence of the lesions, and absence of intense itching. The ring-forms may bear some resemblance to ringworm, but the absence of scales and of the ringworm fungus readily differentiates the two diseases. The vesicular and bullous forms may be confused with dermatitis herpetiformis and pemphigus, but the characteristic distribution and symmetry of the eruption, the presence of other lesions typical of erythema multiforme, the manner in which the vesicles and bullæ are formed, and the mild character of the subjective symptoms, will provide points of difference. In some, fortunately rare, instances of severe generalized types of erythema multiforme with numerous vesicular and bullous lesions, often involving the mucous membranes, the diagnosis from pemphigus may be extremely difficult or even impossible.

Prognosis.—The prognosis is practically always favorable, the eruption disappearing in from two to four weeks, as a rule. It is apt to recur through a period of years, usually in the spring and autumn. In those instances in which the eruption is part of a general systemic disorder, the prognosis depends upon the nature and gravity of the underlying condition.

Treatment.—The disease is self-limited, and internal treatment is chiefly symptomatic, and in most instances is designed to correct gastro-intestinal disturbances, and improve elimination. If the cause is referable to the gastro-intestinal tract, the treatment to be prescribed should consist of several laxative doses of magnesia, or of calomel in divided doses followed by a saline, with salol, sodium salicylate and sodium benzoate when arthritic symptoms are present. Under certain conditions lactic acid bacilli may be of value, but intestinal antiseptics as ordinarily recommended are useless. Intestinal lavage and a carefully arranged diet are of more importance, especially in the prevention of recurrence.

In those cases in which "rheumatic" pains are present in the joints and muscles, the lymphatic structures of the throat should receive consideration as possible sources of infection, The writer has seen several instances in which erythema multiforme was definitely due to tonsillar infection.

The object of local treatment is to relieve itching and burning and subdue inflammation. Sedative evaporating lotions are indicated, such as:

℞.	Phenol	gr. 45	
	Camphor	gr. 20	
	Thymol	gr. 8	
	Amyli	dr. 4	
	Glycerini	oz. 1	
	Ext. hamamelid. dist	oz. 2	
	Spts. vini rect	oz. 1	
	Sol. acidi boric (3 per cent.), q.s. ad	oz. 8	M.

Sig.—Apply frequently and let evaporate.

When the inflammatory symptoms are pronounced a lotion of equal parts of the dilute solution of subacetate of lead and of a saturated solution of boric acid may be applied as a moist compress. If the eruption is extensive, and if vesicles or bullæ are numerous, the patient should be confined to bed. To prevent chilling only a small portion of the surface should be exposed when the lotions or dressings are applied. Ruptured vesicular and bullous lesions should be protected by gauze dressings spread with boric acid or other bland ointment. Lesions on the lips and in the mouth require the frequent use of a cleansing mouth wash, such as the alkaline antiseptic solution, and they may be painted several times a day with a 10 per cent. solution of argyrol. When the erosions are painful Ormsby recommends 15 drops of iodized phenol in one-half glass of water as of benefit.

In periodically recurrent cases a course of intestinal antiseptics and occasional purgation, previous to the usual time of the outbreak, will, Stelwagon believes, sometimes ward off the attack.

Erythema Nodosum.—**Definition.**—Erythema nodosum is an acute inflammatory disease of systemic origin, characterized by the development of painful erythematous nodes or swellings located especially on the shins and forearms.

Symptoms.—The eruption is usually preceded for one or two days by malaise, fever, and joint pains. The systemic disturbance is most often mild in character, but at times the temperature rises to 104°F., the joints are swollen and painful, and the condition resembles articular rheumatism. The skin over the shins and forearms occasionally may be tender in spots or diffusely. Rounded or oval, node-like, painful and tender swellings develop rapidly, varying in size from a cherry to a hen's egg, with a tense and shining appearance. The nodes are fully developed in a few days and then gradually subside during a period of one or more weeks. As involution progresses the nodes frequently soften and become semi-fluctuating, but suppuration or necrosis never occurs, and incision should be avoided. When they first appear the swellings are of bright pink or rose-red color which merges gradually into that of the unaffected skin, and as they involute the color changes from red to purplish, bluish, greenish-yellow, to a brown stain. At times the nodes are hemorrhagic. The lesions vary in number from several to 30, rarely more, and often appear in successive crops of three or four during the course of several days or weeks. The eruption is usually confined to the extensor surfaces of the legs, though it is often present on the forearms and on the dorsal surfaces of the feet and hands. Lesions may occur on the face and buttocks, and rarely on the trunk and mucous membranes. In some cases papular lesions of erythema multiforme type are present.

The course of the disease is apt to vary in that new lesions may continue to appear for several weeks while older lesions fade away, thereby prolonging the disorder beyond its usual period of about three weeks. Recurrences are extremely rare. The constitutional symptoms are of short duration as a rule, but in some instances the fever is continuous, and symptoms indicating visceral or even cerebral involvement are observed.

Etiology.—The disease is most often seen in the spring or autumn, affects females especially, and is relatively frequent in children below the age of 10. Its common association with rheumatoid pains has led some to regard erythema nodosum as a manifestation of rheumatism, especially as the disease in some instances follows a tonsillar or pharyngeal infection, and may be complicated, though rarely, by endocarditis. A similar eruption of nodose swellings has been observed in malaria, syphilis, measles, diphtheria, and after the ingestion of drugs, such as the iodids and antipyrin.

Because of its occurrence in a variety of conditions some writers hold that erythema nodosum is a non-specific cutaneous manifestation of a general toxemia. Rosenow's researches[7] appear to have established a streptococcal type of the disease associated with septic foci. He has isolated a microörganism from the subcutaneous nodes and blood, which, when injected intravenously in animals, has produced hemorrhagic subcutaneous lesions, from which the organism has been recovered.

The frequent association of erythema nodosum with tuberculosis, especially in childhood, has been emphasized by recent writers,[8] though first observed many years ago. The occurrence of this disease in childhood appears to possess an especial significance, for in many instances an attack of erythema nodosum has been followed directly, or within a short period, by the development of an active tuberculous process in the lymph glands, meninges, pleura or other structures. Ernberg,[9] who is chief of the Stockholm Children's hospital, is convinced that erythema nodosum is the manifestation of an anaphylactic process in the course of tuberculosis, the tuberculous focus, usually in the thorax, escaping detection without Roentgen examination. Sequeira[10] has observed lesions of erythema nodosum follow injections of bacillary emulsion for articular and gland tuberculosis. Stokes[11] reports the case of a young girl terminating 30 days after the onset of erythema nodosum in an extensive miliary tuberculosis involving all the viscera, in which there was an apparently exact correspondence of the onset of erythema nodosum with the time of generalization of the tuberculous infection as estimated by the age of the tubercles found at necropsy. This and many other reports furnish clinical evidence, though no conclusive proof, for the belief that erythema nodosum may in some cases be of purely tuberculous etiology. Abt[8] suggests that erythema nodosum, like other infectious diseases, may act by preparing the soil for tuberculous infections, particularly of the miliary type. When erythema nodosum occurs in young children it should be regarded with suspicion, and as perhaps indicative of the change of a latent or unsuspected focus of tuberculosis into an actively advancing process.

Pathology.—The disease is an intense inflammatory process, involving the corium and deeper tissues. There is dilatation of the blood-vessels and lymph spaces, cell infiltration in the papillary and subpapillary layers of the corium, with extravasation of blood, and extensive serous exudation. The veins and lymphatics may at times be blocked by masses of leukocytes.

Diagnosis.—The clinical picture presents such characteristic features that the diagnosis can usually be made without difficulty. Syphilitic nodes develop more slowly, are deep seated, tend to break down, are often painless, and respond promptly to treatment with iodids. While the nodes in congenital syphilis may be numerous, they are often not symmetrical, and are associated with other evidences of the disease. The lesions of erythema induratum of Bazin, a tuberculous process, occur commonly on the calves of the legs of girls from 14 to 20 years of age, are chronic in character, and tend to ulcerate. Bruises and abscesses may resemble the lesions of erythema nodosum, but the latter are usually multiple and symmetrical, are accompanied by constitutional symptoms, and resolve without suppuration. The differentiation from bruises and contusions may have a medico-legal bearing, especially in the case of young children, as pointed out by Ormsby. In rare instances potassium iodid and bromid may produce nodose lesions resembling those of erythema nodosum.

Prognosis.—The disease runs its course in from two to six weeks, and recurrence is rare. In patients with rheumatic symptoms and high temperature, the condition of the heart should be investigated, and in young children the possibility of an association with tuberculosis should be borne in mind.

Treatment.—Rest in bed is essential except in very mild cases. The diet should be light, and in febrile cases liquid. Mercurials and salines to secure free action of the bowels are indicated. Sodium salicylate is indorsed by Duhring, and with sodium bicarbonate is especially useful in cases with joint pains. Salophen, sodium benzoate, and aspirin are of value. Moderate doses of quinin are recommended by Stelwagon, in conjunction with salicylates. The disease is often followed by a secondary anemia which will require its special treatment.

Locally, warm leadwater and laudanum applications, with rest and elevation of the legs during the acute stage, give the best results. Later an ichthyol ointment (3 to 10 per cent.) may be applied under a firm bandage to promote absorption. Similar applications are useful in allaying the pain and swelling about the joints.

Urticaria.—**Definition.**—Urticaria or nettle-rash is an inflammatory affection characterized by evanescent whitish and reddish wheals, varying in size and shape, and attended by itching and stinging sensations.

Symptoms.—Malaise, fever, headache, or symptoms referable to the gastro-intestinal tract may initiate the disorder, or the eruption may appear suddenly without general symptoms. The lesions are firm, usually circumscribed, opaline or pinkish elevations of split-pea to finger-nail size with reddish areolæ, which disappear in a few minutes or several hours, and are succeeded by fresh wheals. Any or all parts of the body may be affected, including the mucous membranes, and at times large areas may be covered by a mottled, sheet-like eruption of coalescent wheals. Gyrate, linear, and band-like forms may be assumed by the eruption.

The itching is intense, and scratching produces new lesions (urticaria facticia) which frequently are linear and correspond to the line of irritation. The rapidity with which the lesions appear and disappear is a characteristic feature. As a rule the eruption fades without leaving a trace, but if scratching has been vigorous excoriations and pigmentation may remain. The course of the disease is most often acute, the attack ending in from one to several days, though recurrences at intervals of weeks or months are not uncommon in sensitized individuals. In other instances the disorder is chronic and new lesions continue to appear indefinitely.

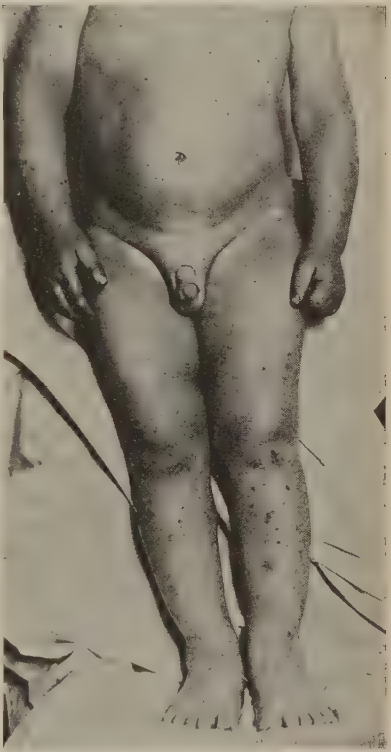

Fig. 40.—Lichen urticatus. (Ormsby and Mitchell.)

Urticaria as encountered in infancy and early childhood differs in many respects from the disease as seen in adults, and is designated *lichen urticatus, papular urticaria,* as or *strophulus infantum.* Although wheals occur, the typical lesion is an evanescent, erythematous, pinkish-red or urticate blotch, only slightly elevated, with a tiny, central, deep-red papule, which persists after the blotch has faded. The papule is the predominant feature of the eruption and may at times develop a vesicle on its summit or be capped by a crust. It usually disappears in from one to several days. The papule may undergo various modifications, at times being a firm, lentil-sized, wheal-like lesion, or when involuting it may become flat, angular and glazed, and resemble the papule of lichen planus. More rarely the papule may become vesicular, or with the surrounding wheal-like area may be rapidly converted into a bulla; such lesions are most often situated on the extremities.

Adamson[12] reports an instance of bullæ on the head and neck occurring in the course of chronic, generalized wheal formation in a baby 17 months old. Eddowes[13] observed the development of keloid-like bands at the sites of urticarial papules in an infant.

The lesions of lichen urticatus have a marked tendency to appear during the night, and during their development are accompanied by intense itching. This leads to scratching, excoriation, and at times to a traumatic dermatitis, and secondary pyogenic infection may take place with the formation of pustules, and enlargement of the lymph glands. The eruption may be sparse or widespread, affecting any part of the body surface, and is most common on the trunk, especially the lower part of the back, and on the extremities. It is never present on mucous membranes. The lesions involute slowly, exacerbations are frequent, especially in the summer months, and the disorder may continue intermittently for several years, though it often terminates at about the age of two years. Constipation or other digestive derangements are frequently associated conditions, and the distress and loss of sleep due to the intense itching further tend to impair the general health.

Etiology.—Like the urticaria of adults, lichen urticatus appears to be due to protein hypersensibility in predisposed subjects. Hypersensitiveness to certain foods may be inherited as well as acquired, and sensitization may occur in nurslings through the agency of the mother's milk. Many articles of food may serve as sensitizing agents, and once an attack has occurred a tendency to the disorder is established, and an eruption is thereafter provoked by minimal causes. In some instances the disorder is traceable to certain articles of diet, eggs, milk, wheat and oats being those to which children are most often sensitive. Schloss' investigations in egg urticaria indicated the anaphylactic nature of at least this one type. Multiple sensitization may be present, especially in adults, and it has been shown that a family history of specific sensitiveness to a certain food not infrequently exists. The studies of Walker, Blackfan and others, with cutaneous reactions to various proteins, of both animal and vegetable origin, have shown that etiologic information of great value in asthma, eczema and urticaria may be obtained by these tests.

In many instances urticaria is an anaphylactic reaction induced by the introduction of foreign proteins in the form of various sera, vaccins, and bacterial products (from focal infections). Urticaria may follow the ingestion of various medicinal substances, among which are quinin, the salicylates, opium, balsam, chloral, iodids, and many of the coal-tar products. Emotional or psychic states, such as anger, fright, shame, sudden grief, will sometimes produce an outbreak, which is attributed by some to interference with the functions of the gastro-intestinal tract, resulting in the production of toxins. Nervous irritability in infants due to teething, the presence of intestinal worms, crying, and the like, may interfere with digestion and be responsible for the eruption. Urticaria may also occur with malaria, hyperthyroidism, jaundice, albuminuria, and various other conditions, and in diseases due to animal parasites. Urticarial wheals may be produced by external causes, such as exposure to heat or cold, bites or stings of insects, contact with caterpillars or nettles, and occasionally by contact of the skin with egg albumin in extremely sensitized children.

Pathology.—The wheal of urticaria is an acute, inflammatory, edematous swelling, with the principal changes in the papillary and subpapillary regions. There is vascular dilatation with rapid exudation of serum and some leukocytes. The effusion is intense and produces a pressure anemia at the summit of the lesion. The lymph spaces also are dilated, and perivascular infiltration is prominent.

Diagnosis.—The diagnosis of urticaria is readily made from the presence of wheals, their ephemeral character, and the itching, but, at times, in the absence of active lesions the diagnosis must be made from the history and the remains of lesions. When only a few scratched papules are present, the diagnosis of urticaria papulosa should not be made until the possibility of insect bites has been eliminated. These are recognized by a central punctiform hemorrhage or blood crust. Urticaria papulosa or lichen urticatus requires differentiation from prurigo, a disease rarely seen in this country though the diagnosis is often erroneously made. In prurigo the eruption involves chiefly the extensor aspects of the limbs, there is marked infiltration and pigmentation which increase strikingly from above downward, there is adenitis, the general health is often impaired, and the disorder persists as a rule after the second year. When the papules of lichen urticatus undergo involution they may become smooth, glazed, flattened and angular, and resemble the papules of lichen planus. In the latter disease the primary lesion is the papule, while in lichen urticatus the papule is preceded by an evanescent urticate tache or blotch of erythema associated with intense itching. Lichen planus is a rare disease in infancy and it is probable that many cases diagnosed as lichen planus infantum are instances of urticaria papulosa.

In cases of urticaria papulosa, especially of the vesicular type, in which the extremities are often chiefly involved, with secondary infection of the lesions and excoriations due to scratching, the differentiation from scabies may present difficulties. In both diseases the itching is worse at night, and urticarial lesions are not uncommon in scabies. The contagious nature of scabies, the presence of scratched arcuate lesions and of intact burrows, and the detection of acari are distinguishing features.

Treatment.—Removal of the cause, if it can be discovered, is the primary indication. In acute urticaria, if seen early, an emetic may be given, or a brisk cathartic, to relieve the stomach and bowels of toxic material. A bland, simple dietary should be instituted and the bowels kept open. In many cases alkalies will prove beneficial, such as the preparations of sodium and magnesium, given frequently. If the attack is persistent salol and charcoal may be added. Severe attacks are rapidly relieved, but only temporarily as a rule, by the hypodermatic use of a solution of 1:1000 adrenalin chlorid solution, which is especially useful when lesions are present in the throat or larynx. Swann[14] advises a dose corresponding to about eight minims for an adult of 140 lb., repeated in 10 minutes. Local treatment in acute attacks may be in the form of baths, lotions or powders. Ointments are not satisfactory agents, as a rule, though zinc oil, with the addition of 1 per cent. each of phenol and menthol, may prove soothing. A general bath or sponge bath with sodium or potassium bicarbonate, or sodium biborate, 6 oz. of the salt to 30 gal. of hot water, usually stops the itching promptly. Starch, bran, or oatmeal baths are often effective. Anti-pruritic evaporating lotions of varied composition are useful. A 1 or 2 per cent. solution of phenol, camphor, resorcin, or liquor carbonis detergens, with glycerin, in 3 per cent. boric acid solution, or in distilled extract of witch hazel with an equal part of boric solution, often gives relief. The addition of zinc oxid or starch may be an advantage at times. A dusting powder, applied after the bath or after the use of a lotion, is frequently of assistance.

In chronic urticaria the condition of the gastro-intestinal tract and the question of elimination are to be thoroughly investigated, and treatment regulated according to the findings. The cutaneous reaction to various proteins should be determined, and though often disappointing the tests may disclose the etiologic factor involved. In many cases, despite careful search, the etiology remains obscure, and the treatment has to be empirical. Calcium lactate, quinin, atropin, pilocarpin, alkaline aperients, foreign protein such as typhoid vaccin by injection, have proved useful in some cases and have failed in others. Patients whose urticaria is due to sensitization to a definite food protein may sometimes be desensitized by administering minute amounts of the protein in increasing quantities. Sutton holds that the possible presence of focal infection is always to be borne in mind.

The treatment of urticaria in infancy and childhood, while based in general on the principles already outlined, is modified by several considerations. Though the dietary is relatively simple, hypersensitiveness to one or more food proteins is not infrequent, and toxic products formed as a result of acute digestive disorders have a considerable share in causing acute urticaria and the more especial juvenile type of papular urticaria. Gastro-intestinal upsets due to teething, and the presence of intestinal parasites, with the attendant nervous manifestations provide indications for treatment directed to special causes. The management in most instances resolves itself into a problem of feeding, and this may tax the skill of the most experienced.

Constitutional disorders, such as rickets, require suitable treatment, and the general health of the child should receive careful attention. Thyroid extract in small doses has proved of benefit in lichen urticatus when the skin is dry and harsh. The writer has also observed a good effect from long-continued small doses of Fowler's solution in cases of papular urticaria of long duration. Warm baths, preferably of oatmeal or starch, followed by dusting powders, are useful in allaying the itching and restlessness. Sedative applications are often required, and the following, recommended by Montgomery,[15] is of value:

℞. Liquor carbonis detergens	30.0
Pulv. amyli	
Pulv. talci veneti —āā	40.0
Glycerini	20.0
Gummi arab	1.0
Liq. plumbi subacetat	4.0
Aquæ	200.0

M. Sig.: Use several times a day as a lotion.

In the vesicular or bullous varieties of urticaria, and in the chronic cases in which a traumatic dermatitis is also present, ointments are useful, such as zinc oxid ointment, with the addition of 2 per cent. of salicylic acid, or boric acid ointment. If secondary infection from scratching has occurred boric acid compresses should be used for drainage, alternating with 2 per cent. ammoniated mercury ointment.

Angioneurotic Edema.—Angioneurotic edema is an acute recurrent inflammatory disorder affecting the skin and mucous membranes, characterized by the sudden appearance of single or multiple, circumscribed, edematous, evanescent swellings of varying size. It is often associated with urticaria, and clinically and histologically the lesions are not essentially different from those of urticaria, except as to size and at times a tendency to recur in the same location. It is rarely attended by other than mild constitutional symptoms, unless the gastro-intestinal mucosa is involved, when fever, colicky pains and vomiting may occur and the condition be mistaken for appendicitis and for renal or gallstone colic. The lesions are usually of considerable size and affect by preference the face, genitalia, and extremities, though they may appear anywhere. The mucosa of the gastro-intestinal and upper respiratory tracts may be involved, and in the latter location, suffocative attacks with death have often occurred, especially in the hereditary type.

Etiology.—The disease has been observed in infants six weeks old, but is most frequent between the ages of 10 to 40 years. The exact cause is at present unknown. Darier states that the etiology is the same as that of chronic urticaria. Heredity is an important factor, and nervous instability also appears to be a predisposing cause.

Prognosis.—The prognosis should be guarded as the disorder may recur for years, and edema of the larynx is a menace in the hereditary form.

Treatment.—The treatment, both local and general, is essentially that of urticaria. Calcium salts given over a prolonged period are advocated. Adrenalin will often relieve the acute swelling.

Prurigo.—Definition.—Prurigo is a chronic inflammatory disease of the skin, commonly beginning in infancy or early childhood, continuing for years or through a lifetime, and characterized by the presence of recurring, discrete, firm, pale papules, which itch intensely. A mild and a severe form are recognized, the latter being the prurigo originally described by Hebra. The disease is rare in this country and is chiefly seen in Austria and eastern Europe.

Symptoms.—As a rule prurigo begins during the first year of life as an urticaria or strophulus, attended by severe itching, and assumes the papular form in the second year. Some observers[16] maintain that the earliest lesions are always papular and not urticarial. After a year or two the disorder is usually fully developed. On the extensor surfaces of the extremities, on the trunk, the forehead, neck and face, there is an eruption of discrete, pinhead-sized or slightly larger, rounded or conical, firm papules, pale red or of the natural color of the skin. They are

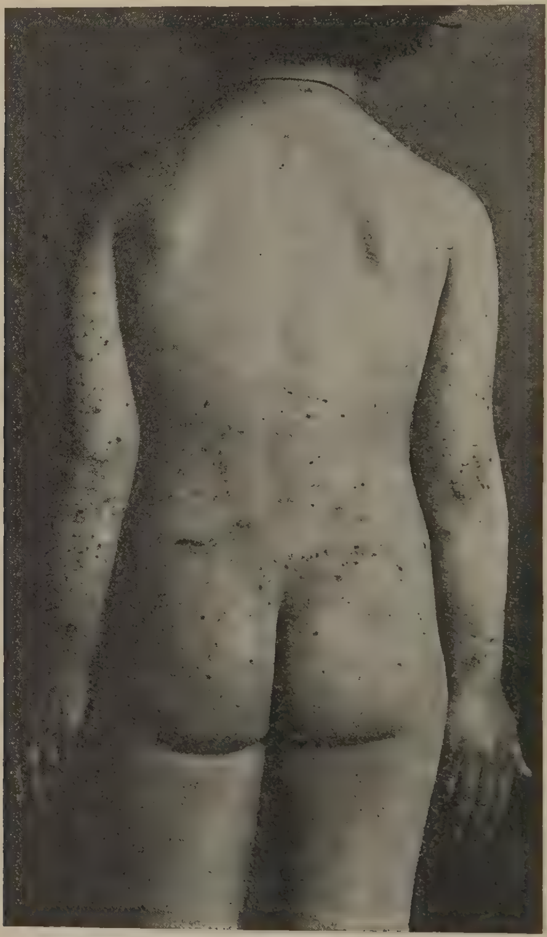

Fig. 41.—Prurigo. (Fordyce and MacKee.)

intensely pruritic, and as a result of incessant rubbing and scratching the skin develops crusts, linear or follicular excoriations, pustules, dense infiltrations, and eczematous patches. Finally, the skin becomes thickened, hard, tense and lichenified, with the natural furrows deepened, and this cutaneous infiltration is characteristic in that on palpation it increases in proportion to the distance from the scalp, being most marked on the legs. The face often assumes a senile appearance. Pigmentation is a constant feature, and varies in color from a dirty-gray to brown, and frequently develops early in the disease. The superficial lymph glands, especially the axillary and inguinal groups, are always enlarged, and may suppurate.

The distribution of prurigo is one of its most striking features. The lesions occur chiefly on the extensor surfaces of the legs and arms, buttocks, lower part of the abdomen, over the sacrum, and less frequently on the upper part of the trunk, cheeks, sides of the neck, and forehead. They are practically never present in the groins, axillæ, and the popliteal and cubital spaces, though a secondary dermatitis may invade these areas.

The physical discomfort, insomnia, and constant nervous strain to which patients with prurigo are subject reduces them mentally and physically, and malnutrition, lowered vitality, and mental depression are common sequels.

The course of the disease is remittent, and intervals of comparative comfort alternate with marked recrudescences, especially in the cold season, until toward puberty or about the age of 20 the disease loses much of its intensity and resembles a chronic eczema. The mild form of prurigo, as distinguished from the severe form of Hebra, is less intense in all of its manifestations, and in often amenable to treatment. It maintains its mild character throughout its course, while a prurigo which begins with severe symptoms may persist in this form throughout life.

Etiology.—The disease is more frequent in males, is not contagious, and occurs almost exclusively among the poor. The actual cause is unknown, though heredity and a neurotic basis are considered as predisposing factors. Prurigo appears to be closely analogous to urticaria papulosa. The assumption that cutaneous hypersensitiveness, in a predisposed individual, due to an autogenous toxin perhaps alimentary in origin, is the cause of prurigo has much in its favor, and finds support in the researches of Hans Schwartz.

Pathology.—The histologic changes are chiefly those of chronic inflammation and are practically identical with those seen in chronic papular eczema.

Diagnosis.—The disease is to be distinguished chiefly from papular eczema with xeroderma, by the character and distribution of the lesions, by their uniform type, the infiltration of the skin, the marked adenopathy, the origin in early childhood and the chronic course, and the rarity of prurigo in this country. Its differentiation from lichen urticatus has been discussed under urticaria. Parasitic affections and urticaria are readily differentiated by the history and the character and distribution of the lesions in prurigo.

Treatment.—Proper hygiene, nourishing food, fresh air, cod-liver oil and iron, and often rest in bed, are essentials in the management of the disease. Careful inquiry should be made into the digestive and renal functions and the condition of the teeth. Eliminative treatment by catharsis, intestinal irrigation, and diuresis, and the promotion of sweating by hot packs (and pilocarpin given hypodermically in older children) are useful and often provide symptomatic relief. Arsenic is of little or no value. Thyroid extract and phenol have been effective in some cases. Locally, Wilkinson's ointment of sulphur, tar and green soap is of distinct value. Kaposi favored betanapthol, 1 to 2 per cent. in petrolatum, for children, rubbed in every night, with a bath every other night, but toxic symptoms have often followed the use of this chemical. A good procedure is that of a daily hot bath, with the addition of sodium bicarbonate (4 oz. to 30 gal. of water), or of Vleminckx's solution (2 to 4 oz.), followed by thorough inunction with a modified Wilkinson's ointment (sulphur sublimat., ol. rusci āā 15.0, saponis mollis, adipis āā 30.0, cret. preparat. 3.33) reduced in strength according to the age of the patient and the condition of the skin. It should be remembered that when tar is used over the general surface, absorption may take place with the production of headache, fever, vomiting and diarrhea, which calls for immediate discontinuance of the drug. When considerable dermatitis is present mild ointments are demanded as a preliminary to other treatment.

Urticaria Pigmentosa.—**Definition.**—Urticaria pigmentosa or xanthelasmoidea is a chronic, inflammatory disease of the skin, beginning usually in early life, characterized by persistent pigmented macules and nodules. The disorder has been observed chiefly in Great Britain, and is comparatively rare in this country.

Symptoms.—The disease usually begins in the first year of life, and is very rarely congenital,[17] and it may first appear after puberty. The lesions tend to appear suddenly in crops, may be few in number or profuse, and are situated chiefly on the trunk, especially on the back, and on the proximal parts of the limbs, and on the neck, face, and scalp, but rarely on the palms and soles. The early lesions are wheal-like, pinkish, smooth and soft, usually pea size or slightly larger, and are rounded or often oval in contour with the long axis directed downwards on the extremities, transversely on the neck, and downwards and forwards on the trunk (MacLeod). In exceptional instances the lesions are vesicular or bullous.[18] A pathognomonic feature is the congestion, swelling, and enlargement of the lesions which follows when they are irritated by friction. Itching is often absent, and as a rule is not pronounced, and dermatographism is usually present.

The urticarial early phase of the lesion is transient and is succeeded either by persistent brownish-yellow stains and flat or slightly elevated pigmented macules of the same shape and size as the original lesion, or by nodules which remain indefinitely. A mixed type of macular and nodular lesions is frequent. In the macular variety the lesions are of larger size, and may coalesce and form large, irregular patches, which sometimes cover large areas of the cutaneous surface. The nodules are at first reddish-yellow, solid and indurated, and bear a close resemblance to the lesions of xanthoma, but in time become brown-red or yellowish-brown, with a smooth, roughened or wrinkled surface. Individual nodules may persist for many years, while others gradually involute and disappear leaving pigmented and at times atrophic spots. Fresh outbreaks occur at irregular intervals and the disease is prolonged for years, though it usually subsides at puberty. Throughout its course the formation of wheals upon the pigmented lesions by friction is a characteristic clinical feature. Pigmented patches have been observed on the buccal mucosa in several instances, but their connection with the disorder has not been proved. The general health is not affected unless itching is pronounced. General adenopathy has been observed in a number of cases, the glands being firm and shot-like, especially in the post-cervical group.

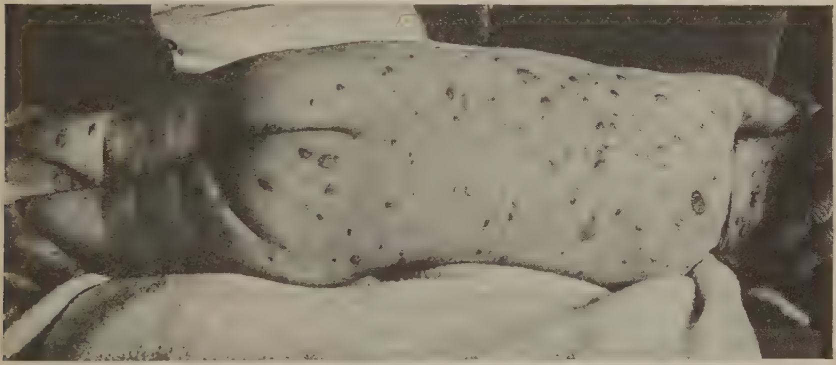

FIG. 42.—Urticaria pigmentosa. (Fordyce and MacKee.)

Etiology.—The cause of the disease is unknown. It has developed immediately after vaccination, varicella, measles, emotional disturbances, such as shock or fright, and after cutaneous irritation by chemicals, and Little[19] correlates these as determining factors with an apparently congenital tendency to over-production of mast-cells observed in the skin of patients affected with this disease. Knowles[20] believes the cause to be a toxin of unknown nature acting upon a congenitally abnormal skin. Others consider the disease as related to nevi.

Pathology.—The characteristic feature is an abundant infiltration of the corium with closely packed mast-cells, arranged in rows and columns between the collagenous bundles, and deposited about the dilated blood-vessels, and the hair-follicles and sweat-glands. Mast-cell infiltration also has been found in the apparently normal skin in these cases, which is suggestive of a congenital abnormality. Pigment cells containing melanin are found in the basal layer of the epidermis and in several of the layers above it, and in the papillary body.

Diagnosis.—Urticaria pigmentosa is to be differentiated from urticaria with pigmentation by its origin in early infancy, the persistence of the lesions and their conversion into wheals by friction. The lesions of xanthoma are distinguished by their development at a later period than infancy, by their location, the absence of wheal formation and itching and by their peculiar chamois-yellow color. In two cases reported by Wise, diagnosed clinically as urticaria pigmentosa, the histologic examination proved the condition to be endothelioma.

Treatment.—Itching may be relieved by the use of the antipruritic applications referred to in ordinary urticaria. Internal medication is without effect, though attention to the diet and treatment directed to relief of gastro-intestinal or other disturbances assist in improving the patient's condition.

Hydroa Vacciniforme.—**Definition.**—This disease, also known as recurrent summer eruption or hydroa estivale, is a recurrent vesicular eruption, which appears chiefly in the summer season, in young males, and affects only the exposed portions of the skin. It usually begins during the second or third year of life and gradually subsides shortly after puberty, although it has been known to develop as late as the twenty-sixth year. The disease is most frequent in boys, though MacLeod believes it to be equally common in both sexes.

Symptoms.—The eruption is usually symmetrical and shows a strong predilection for the uncovered parts—the bridge of the nose, cheeks, ears, sides of the neck, backs of the hands and forearms, and less often the legs. Hyde has observed lesions on the cornea. The eruption may begin as pinhead to lentil-sized red macules or papules with vesicular summits; these subside rapidly, with the formation of a small scale or thin crust, and leave a small, shallow scar or pigmented spot. In the more severe type, as originally described by Bazin, the first lesions to appear are red macules or elevations, upon which tense, rounded vesicles rapidly develop, either singly or grouped as in herpes. The vesicles are of pinhead to large pea size, and often coalesce into irregular bullæ, which may be ½ in. in diameter, with milky or puriform contents. After the second day the vesicles may dry and become umbilicated, or they may rupture and form crusts. In the larger vesicles or bullæ the center often sinks down into a dark colored crust, which is surrounded by a vesicular or pustular border and a reddened areola, producing a close resemblance to a vaccin lesion. Within three or four days the vesicle is converted into an adherent crust, which on falling leaves an atrophic scar like that seen after variola. Individual lesions last for several days, but an attack is often prolonged for weeks by the appearance of renewed crops at irregular intervals. The recurrence of lesions from year to year upon the same sites ultimately results in considerable atrophic scarring and disfigurement, which is most marked on the ears, nose, and finger joints where the skin is thin and in close apposition to the underlying cartilage and bone. The eruption usually is preceded by slight indisposition, and by sensations of burning or pain at the site of the lesions, which persist until the lesions are fully developed. Itching is not pronounced as a rule.

Hydroa Puerorum.—This affection was originally described by Unna and bears some resemblance to hydroa vacciniforme, though Haase and Hirschler[21] consider it an entity. The disease occurs only in boys and begins in the first year of life, each attack lasting about two weeks. The lesions are erythemato-vesicular, the vesicles coalesce to form bullæ, and involute without scarring. They develop on any part of the body, and may be profuse on covered parts. The attacks are independent of external or seasonal influences, and cease spontaneously at puberty.

Etiology.—Recent investigations[22] establish the photo-actinic origin of many cases of hydroa vacciniforme. The eruption is produced by exposure of the skin to the influence of the ultra-violet constituents of the solar spectrum in susceptible individuals. The susceptibility appears to be intimately associated with the presence of hematoporphyrin or of porphyrinogen in the urine, and the experimental production of lesions in man and in animals supports this view. These compounds are products in the metabolism of hematin to bile-salts, the primary factor being a perhaps congenitally disordered function of the liver.

Pathology.—The histopathology is that of an acute inflammatory process beginning in the epidermis and upper corium, followed by vesicle formation in the rete, and later by a circumscribed necrosis of the entire rete and of the corium to a considerable depth.

Diagnosis.—The peculiar distribution of the eruption, its course, the vacciniform type of lesion, the age of the patient, and the scarring, should be sufficient to differentiate it from erythematous lupus, erythema multiforme, impetigo, xeroderma pigmentosum, and dermatitis herpetiformis, with which it might be confused.

Treatment.—Avoidance of exposure to the sun, and to strong winds in some cases, is essential. Protective coverings, such as veils, may be useful. Ointments or pastes containing substances which are absorbents of ultra-violet rays, such as aesculin, derived from walnut juice, have been suggested. Ichthyol (2 per cent. or more) in paste has been beneficial in some cases. The local treatment includes compressing of the lesions with dilute lead solution or aluminum acetate solution, and puncturing of the vesicles, which are then dressed with boric acid or ammoniated mercury ointment. Crusts may be removed after softening with an oil, and the exposed surface is then dressed with an antiseptic ointment. The internal use of quinin has been especially recommended, but its value is doubtful.

Lichen Planus.—Definition.—Lichen planus is an inflammatory dermatosis, characterized by small, angular, flat-topped, red or violaceous, often glistening papules, which tend to coalesce into scaly patches.

Symptoms.—The primary lesions are pinpoint to pinhead-sized, firm, polygonal or faceted, flat-topped papules, at first pinkish-red and later violaceous in color. The surface is often glazed, and in older lesions shows milky striæ. A small central depression or dell is present in many lesions, while others may have central horny plugs. The lesions are often discrete and scattered, but tend to coalesce into angular, linear, or irregular patches, covered with fine, closely adherent scales. Annular or circinate patches may be formed, and the lesions may follow the line of a scratch-mark. When the papules or patches involute a pigmentation of brownish or blackish hue often remains, especially on the wrists and legs. The favorite sites of lichen planus are the flexor surfaces of the wrists and forearms, the inner aspects of the knees and thighs, and the legs above the ankles The eruption is often more or less symmetrical, and in extensive cases may affect large areas of the cutaneous surface. It rarely appears on the face, scalp, palms or soles. Lesions on the tongue and mucous membranes of the mouth and lips are frequently present as whitish patches or streaks, and on the glands or vulva as grayish, angular patches or as typical, though thinned and flattened, lichen planus papules. The cutaneous lesions at times also exhibit various modifications, and may be verrucous, vesicular, bullous, and spinous.

The disease may rarely appear in an acute form, with constitutional symptoms of greater or less severity, and become generalized in a few days. Usually the course of the disease is chronic, the eruption appears gradually, and tends to persist, though it may disappear spontaneously. Its duration is variable, lasting for months or rarely years, through the continued appearance of new lesions. Second attacks are rare. Subjective symptoms of itching or burning are usually present, and though often slight, may sometimes cause extreme suffering. As a rule, the general health is not impaired unless the itching interferes with sleep and rest. Nervous irritability is sometimes present.

Lichen planus is of rare occurrence in childhood, and it is probable that many of the cases diagnosed as lichen planus are instances of lichen urticatus. Crocker's lichen infantum was later recognized by him as a subsiding stage of papular or vesicular miliaria rubra. However, undoubted instances of lichen planus have been observed at every period during childhood, beginning with the first year of life, though no congenital case has been recorded. The disease in children does not differ in its course, distribution or clinical appearance from the disease as seen in adults, though linear forms are relatively frequent and the face is more often affected. The mucous membranes of the mouth and genitals appear, according to Kiess, to be involved less often than in adults.[23]

Etiology.—The cause of lichen planus is unknown. The prevailing view is that toxemia and nervous disturbances are essential factors in the causation of the disorder. Others, among them the writer, believe that there are good reasons for regarding lichen planus as a microbic disease.

Pathology.—The histopathology is characteristic and fairly constant in all types. The papule is usually situated about a sweat-duct. There is a circumscribed cellular infiltration in the papillary layer of the corium, of connective-tissue cells and lymphocytes, with edema. In the epidermis there is marked hypertrophy of the rete mucosum (acanthosis), of the granular layer, and the stratum corneum (hyperkeratosis), with some colloid degeneration.

Diagnosis.—The characteristic features of the lichen planus papules, their peculiar distribution, and the absence of moisture at any stage will serve to distinguish this disease from papular eczema. In guttate psoriasis the lesions are scaly from the beginning, the scales are abundant, and when removed there is punctate bleeding. The miliary papular syphiloderm is to be differentiated by its color, distribution, associated adenopathy and other symptoms, and the presence of a positive serum reaction. The pseudo-papules observed in infiltrated patches of dry, chronic dermatitis may simulate closely the papules of lichen planus. They owe their angular, mosaic-like appearance to the exaggerated markings of the lines of the skin. The differentiation from lichen urticatus or urticaria papulosa may be one of extreme difficulty. When the papules of lichen urticatus involute they may become smooth, glazed, flattened and angular, and closely imitate the papules of lichen planus. However, in the latter disease the papule is the primary lesion, while in lichen urticatus the papule is preceded by an evanescent urticarial spot or blotch of erythema associated with intense itching. Excoriations due to scratching may be present in lichen urticatus, whereas scratch marks are decidedly uncommon in lichen planus.

Treatment.—This consists in attention to the gastro-intestinal tract, good hygiene, and the administration of cod-liver oil and of tonics when indicated to improve the general health. Arsenic is a valuable remedy in the subacute and chronic cases, though it often fails. Mercury is held by many to be superior to arsenic, and is given as the protoiodid or biniodid by mouth, or as the bichlorid by intramuscular injection. In acute cases alkaline diuretics are of value. Daily warm baths in oatmeal water, followed by a camphorated dusting powder, have a soothing effect in acute and extensive cases. The calamine emulsion, with 1 per cent. phenol added, is useful in relieving itching, or an ointment may be used containing 1 per cent. of phenol and menthol and 2 per cent. of ammoniated mercury. Infiltrated lesions often involute rapidly after exposure to *x*-rays.

Lichen Spinulosus.—Lichen spinulosus, also called lichen pilaris, is a rare condition chiefly seen in children, in which the characteristic lesions are minute acuminate papules, each having a projecting horny spine up to 1/8 in. in length. They appear in crops and tend to form somewhat symmetrical patches, though many remain discrete, and occur chiefly about the back of the neck and shoulders, the buttocks, trochanteric regions, abdomen, thighs, popliteal spaces, and extensor surfaces of the arms. At first the papules are pink or red, and later assume the color of the normal skin. The lesions may persist indefinitely when untreated.

Filiform spines are also observed in association with lichen planus, lichen scrofulosorum, seborrhoic dermatitis, and the lichenoid trichophytids described by Jadassohn in 1911. Several cases have been recorded[24] recently in each of which the development of lichen spinulosus on the cutaneous surface was preceded for several years by folliculitis decalvans of the scalp.

Etiology.—The cause is unknown. A toxic origin is suggested by Adamson, supported by the occurrence of lichen spinulosus lesions in the toxi-tuberculids and tricophytids, and in their association with folliculitis decalvans, a chronic infective process.

Pathology.—Adamson found that a horny plug distended the pilo-sebaceous follicle in its upper third and extended outwards as a spine. The hair-bulb was unaltered, the sebaceous glands were atrophied, and the connective tissue cells were slightly increased at the follicle neck and near the papillary vessels. No microörganisms were found.

Diagnosis.—Lichen spinulosus requires differentiation from keratosis pilaris in which the lesions are diffuse, do not form patches, and involve the extensor surfaces of the extremities. The lichenoid tricophytid is found associated with ringworm of the scalp, usually kerion celsi. Pityriasis rubra pilaris may be distinguished by its inflammatory character, wide distribution, scaling, and the presence of lesions on the dorsal surface of the fingers.

Treatment.—The disease responds readily to applications of tincture of green soap followed by salicylic acid and resorcin in ointments, or to preparations containing tar. Without treatment the lesions may persist indefinitely.

Pityriasis Rubra Pilaris.—**Definition.**—Pityriasis rubra pilaris of Devergie (lichen ruber acuminatus of Kaposi) is a chronic, mildly inflammatory disease, in which the lesions are small, conical, red and scaling papules with horny centers, situated at the openings of hair-follicles, and often forming extensive scaling patches.

Symptoms.—The disease usually develops gradually, though the onset may be rapid, with or without mild systemic symptoms, and often appears first as a seborrhea sicca of the scalp, with red scaly patches on the forehead or face and often on the palms and soles. The characteristic papules then appear on the dorsum of the fingers and hands, on the neck, abdomen, forearms, or other regions. The papules are seated at the mouths of hair-follicles and are conical or acuminate, dry and hard, with a central horny plug, usually pierced by a lanugo-hair, or showing the end of a broken hair. They are of a pinkish-yellow or pale red color. The lesions usually are abundant and closely grouped, forming large patches which give a nutmeg-grater-like appearance and feel, or they may coalesce and form extensive reddened infiltrated areas, with exaggeration of the natural lines of the skin. In these areas there is a profuse desquamation of fine, branny, grayish scales. The palms and soles show diffuse reddening and infiltration, with exaggeration of the normal lines, and appear as though brushed with chalk or gypsum When the eruption is extensive the face is usually involved, and is red, infiltrated, and covered with branny, greasy scales, or less often, partly encased in a white, mortar-like cast. Ectropion of the lower eyelids may occur due to tension of the dry and infiltrated skin. An important diagnostic feature is the presence of numbers of tiny, horny, black, conical plugs occupying the site of the hair-follicles on the dorsal surfaces of the first and second phalanges of the fingers. The nails are often affected and become friable, striated, and roughened.

Moderate itching may be present, and the usual complaint is of a sensation of dryness and contraction of the skin. The general health is not impaired in the earlier stages, even in generalized cases, but sometimes failure of nutrition and marasmus set in later, and death ensues.

The course of the disease is chronic, with periods of remission and sudden extensions. At the onset it may remain confined to a few areas for months or years, but its tendency is to become generalized and even universal, and to persist indefinitely.

Etiology.—The cause of the disease is unknown. It may occur at any age, and often begins in early childhood, though more commonly in the second decade of life. Whitehouse has reported a case beginning at the age of one year. The majority of cases seem to be in males. It is sometimes found in association with psoriasis, and is regarded by some as a follicular phase of psoriasis. The evidence for a tuberculous origin advanced by Milian is not conclusive.

Pathology.—The histopathology shows that the horny papule is formed by a hyperkeratosis of the upper portion of the hair-follicles, with a hyperkeratosis of the entire epidermis and a mild inflammatory process in the corium. There is no alteration of the sebaceous or coil glands.

Diagnosis.—The characteristic features of pityriasis rubra pilaris are the horny follicular papules pierced by hairs, seen in nearly all cases on the backs of the fingers, the nutmeg-grater-like papular eruption on the abdomen and other parts, the red, infiltrated, scaling patches, and the palmar and plantar thickening. Keratosis pilaris is limited to the extensor aspects of the extremities. In lichen planus and psoriasis the lesions have a different distribution, the palms and soles are rarely affected, the eruption is seldom as extensive, and the acuminate papules or the nutmeg-grater-like appearance are not present.

Prognosis.—The disease is chronic, and though periods of remission may take place, it almost invariably recurs. After several years it may disappear spontaneously, but its tendency is to persist. In exceptional cases it may prove fatal.

Treatment.—There is no specific remedy and internal treatment should be directed to meet the indications in the individual patient. Cod-liver oil and a nutritious diet with tonics are often useful. Arsenic has been recommended, but is useless, and may be harmful, as also arsphenamin. Pilocarpin, thyroid extract, injections of tuberculin, and mercury have been advocated, but the results are inconstant. Ormsby has observed marked amelioration following the combined use of arsenous trioxid and protoiodid of mercury, together with external applications.

The local treatment includes the use of alkaline, oatmeal or bran baths, followed by the application of bland ointments (equal parts of lanolin, vaselin, and olive oil) or of ointments containing from 1 to 5 per cent. of salicylic acid. A glycerite of starch cream for the face and hands is useful to relieve tension and dryness of these parts. Radiotherapy may produce temporary improvement, and Sibley[25] records a cure with electric-light baths.

Pityriasis Rosea.—**Definition.**—Pityriasis rosea is an acute, self-limited inflammatory disease, characterized by an eruption of pinkish, scaling macules, which form oval or circinate patches, situated chiefly on the trunk.

Symptoms.—The disease is often preceded by a circinate, erythemato-squamous, primary or "herald" patch, situated usually on the trunk, and resembling a patch of trichophytosis. After one or two weeks an eruption develops, often with the suddenness of an exanthem, and accompanied at times by mild constitutional symptoms. When fully developed the eruption consists of numerous pinhead to small-coin-sized or larger, rounded or oval macules or maculo-papules, with indistinct margins, tending to enlarge by peripheral extension and to coalesce into irregular patches. They are covered with thin wrinkled scales, and vary in color from a yellow or salmon shade to pale red. Among the larger lesions many are circinate, with slightly elevated, pinkish, scaly borders, and fawn-colored, finely wrinkled centers. The primary or "herald" patch often remains recognizable for several weeks as the most conspicuous and largest of all the lesions. Enlargement of the post-cervical lymphatic glands is often present, or there may be a general adenopathy. Itching is not a pronounced symptom, and is often absent. In the majority of cases the eruption is most profuse on the trunk, and it generally begins about the neck and upper thorax and spreads downward to the abdomen, arms and thighs. It may be confined to a limited area such as the thighs, is rarely present on the face, hands and feet, but may involve any part, including the scalp and penis. The mucous membranes appear to be exempt. The evolution of the eruption occurs in successive crops, so that lesions in all stages of development may be present at one time. In most cases the eruption disappears spontaneously in from three to six weeks, without leaving any trace, but it may last for several months. Recurrences are rare.

Variations in the eruption are not uncommon, and it may remain almost entirely papular throughout its course, only a few patches or circinate lesions being present. In children the eruption is often chiefly papular, and sometimes may exhibit vesicular elements, but characteristic oval or circinate patches can always be detected at some period of the disease. In children there is also a tendency of the eruption to remain limited in its distribution.

Etiology.—The cause of pityriasis rosea is unknown. It occurs with especial frequency in the spring and autumn months. Little's[26] analysis of 146 cases shows that 22 per cent. occurred between the ages of 5 and 10 years, and 44 per cent. under the age of 15. The disease has been observed in infancy and in old age, but is perhaps most frequent in early adult life. It is equally common in either sex. The disease presents features which indicate that it is feebly infectious and perhaps allied to the exanthemata or to the toxic erythemata.

Pathology.—In the early stages there is dilatation of the vessels, cellular infiltration and marked edema in the papillary and subpapillary layers of the corium; later the edema extends into the epidermis, the prickle cells proliferate, and cornification is impaired, producing scaling. If the edema is marked the prickle cells undergo spongy changes and microscopic vesicles form beneath the horny layer, which exfoliates later.

Diagnosis.—Pityriasis rosea is differentiated from seborrhoic dermatitis by the distribution of the latter over the scalp, face, sternal and inter-scapular regions, and the yellow color, coarse and greasy scales of its lesions. There are border-line cases in which the differential diagnosis is almost impossible. Patches of psoriasis are elevated, sharply outlined, and slow in development, the scales are coarse and silvery, and the sites of predilection are the scalp and extensor surfaces. The discoid papulo-squamous syphilid may resemble pityriasis rosea closely, but is distinguished by its infiltration, dull tint, slow development, and the presence of other symptoms of syphilis. In ringworm of the body the lesions are seldom numerous, they tend to be large and circular, with clear centers, and the trichophyton fungus is present in the scales.

Treatment.—The disease is self-limited, and it is questionable if any treatment, external or internal, influences its course. Salicin is advocated by English dermatologists. Locally soothing applications may be used, such as the zinc and calamin emulsion or cream, with the addition of 2 per cent. of phenol in pruritic cases, followed by a bland dusting dowder.

Psoriasis.—Definition.—Psoriasis is a chronic inflammatory disease characterized by red macules or flat papules, and well-defined red patches, covered by silvery-white, imbricated scales, and occurring on the extensor surfaces by preference.

Symptoms.—The elementary lesion of psoriasis is a pinhead-sized, red, infiltrated, flat or acuminate papule, capped with whitish, mica-like scales. When the scales are completely removed a bright-red surface is exposed, dotted with minute bleeding points which correspond to the tips of the papillæ beneath. The papules slowly enlarge at the periphery and form round or oval, slightly elevated, infiltrated, circumscribed, scaly patches, which retain all the characteristics of the original lesion. Larger patches are formed by increase in size of the original papules or by the coalescence of smaller patches, whereby various forms and configurations are produced, with a general circular arrangement. Various descriptive terms such as punctate, guttate, discoid or nummular, circinate, gyrate, diffuse, and universal are used to designate the manifold configurations and sizes assumed by the psoriatic lesions. But, whatever their size, shape or location may be, the original type of the inflammatory, scaling lesion is maintained, and they never become vesicular or pustular, and only as a result of secondary changes may be moist. The eruption is often symmetrical in distribution, and it appears by preference on the extensor surfaces of the extremities, especially about the knees and elbows, the scalp, lumbo-sacral region, upper part of the thorax, face, and abdomen. The lesions are usually numerous on the trunk and extensor surfaces, and in some cases large areas of the skin are involved. In rare instances the eruption is universal and the condition is indis-

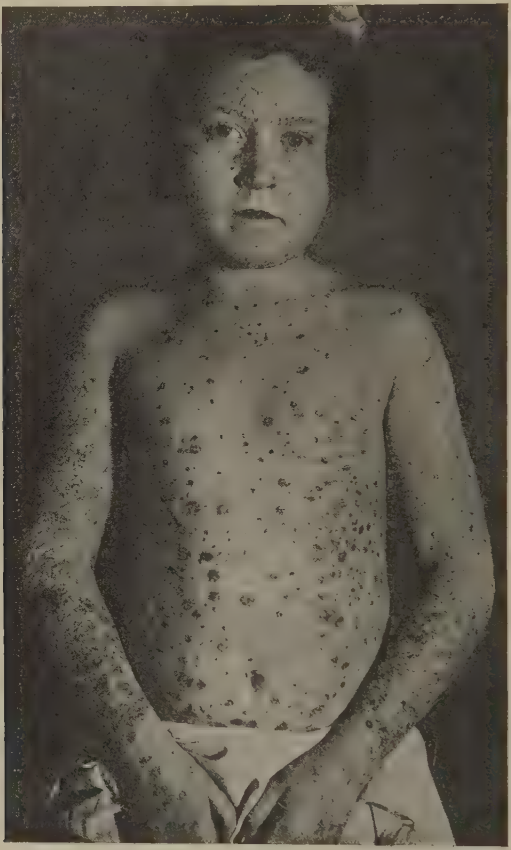

Fig. 43.—Psoriasis. (Fordyce and MacKee.)

tinguishable from general exfoliative dermatitis. The palms and soles are rarely affected, and it never appears on the mucous membranes. In many cases the nails are involved and become thickened, opaque, pitted, irregularly laminated, and brittle, with often an amber-like change. In children the more pronounced types of the disease are rarely seen, the lesions usually being small, widely distributed, and discrete, except at the knees, elbows and in the lumbo-sacral region where they form patches.

The course of psoriasis is chronic. The lesions usually disappear as a result of treatment or spontaneously; and often during acute febrile and other intercurrent diseases, but recur sooner or later. In the same individual the number, size, character and location of the lesions may undergo continual variation, and in others the eruption may be limited for years to one or more areas, as the elbows and knees. Recurrences may be extensive, or differ considerably in the number, character and distribution of the lesions from those of previous attacks. The intervals between attacks vary from a few weeks to several months, and are seldom longer than a year. In many patients the eruption disappears either partially or wholly during the warm months, and reappears in cold weather, or less often, the reverse occurs. Involution of the patches begins in the center and progresses slowly until only slight, temporary pigmentation is left.

The subjective symptoms are slight, except in acute types when the itching may be severe. The general health is not affected.

Etiology.—The cause of psoriasis is unknown. It is a common disease and may occur at any age. Though it frequently begins between the ages of 5 and 15, it occurs most often in the second and third decades of life, and rarely begins after 50. It has been observed in an infant six days old, and in a considerable number under one year, but is rare in infancy. Sex and social condition have no bearing on the etiology, though an inherited predisposition appears to be a factor in some cases. It is not contagious, and the microbic origin of psoriasis, though reasonable, remains to be proved. The disease may develop after vaccination, and after other local injuries during its periods of activity, and has been ascribed to microbic inoculation, a view which is untenable. Metabolic studies by Schamberg indicate an abnormal nitrogen retention, and Darier states that a diet especially rich in albuminoid substances seems to be capable of favoring the first appearance, or at any rate the eruptive outbreaks, of psoriasis.

Pathology.—The chief changes observed are hyperkeratosis and parakeratosis in the horny layer, microscopic abscesses formed by migrated leukocytes in the scale and rete, hyperplasia of the rete mucosum except in the portion overlying the papillæ, with enlargement of the rete pegs, and edema. In the corium there is vascular dilatation, edema of the collagen, and perivascular cellular infiltration, and the papillæ are elongated and thickened corresponding to the rete pegs. There is a difference in opinion as to whether the initial change is in the epidermis or in the corium.

Diagnosis.—The disease usually presents such characteristic features that it is recognized with ease. Atypical and poorly marked cases may offer difficulties. Seborrhoic dermatitis, syphilis, eczema, and pityriasis rosea are the diseases that exhibit the closest resemblance to psoriasis.

In seborrhoic dermatitis the scales are less abundant, smaller, and greasy, and the base of the lesion is moist, less congested, and shows no bleeding points. However, there are cases of psoriasis in which the scales may be greasy and the surface beneath them moist, and sometimes the two diseases may be associated. The lesions of seborrhoic dermatitis are rarely seen on the elbows and knees, and in children occur chiefly on the scalp and forehead, behind the ears, in the axillæ, and in the sternal and interscapular regions. In infancy the folds of the skin are often invaded and the eruption is then moist or exudative.

In eczema the flexor surfaces, the folds and depressions of the skin, and the skin adjacent to the mucous outlets are involved by preference. The patches usually are not symmetrical, are often traumatized because of itching, they are at some time moist, exudative, or crusted, and the scales are sparse, small, yellowish, and dull. Patches of squamous eczema are usually less numerous, larger, and have illy defined margins which fade out into the normal skin. However, in the delicate skin of children, especially in the napkin area, or as the result of local irritation or of infection, patches of psoriasis occasionally may become acutely inflammatory and indistinguishable from eczema.

The scaling syphilids may resemble psoriasis very closely, but the presence of other evidences of syphilis, such as mucous patches and condylomata, the occurrence of lesions on the palms and soles, their uniform size and character, the dirty-yellowish, scanty, crust-like scales overlying an infiltrated, elevated, dull-red papule, are distinguishing features. Children affected with syphilis are impaired in health, cachexia may be marked, and the skin often hangs in loose folds, though in some cases only slight disturbance of nutrition is present. If the diagnosis cannot be made from the clinical appearances, the result of the Wassermann serum reaction may provide corroborative evidence.

In pityriasis rosea the lesions are more superficial, more rapid in evolution, and less inflammatory. They are most profuse on the trunk, oval in contour, have fine scales, and the center is of a tawny or salmon color and often finely wrinkled like cigarette paper. The disease is of short duration and rarely recurs.

In trichophytosis corporis, or ringworm of the body, the lesions are few in number, circular, often exhibit vesicles at the margin, tend to clear in the center, and carry the causative fungus in the scales.

Treatment.—There is no specific remedy for psoriasis. The lesions usually disappear in response to treatment, both external and internal, but they recur, and may not yield again to the same treatment or to that which has been successful in another individual. The disease is resistant to treatment, though experience has shown certain empiric measures to be of value. Attention should be given to any defects of health, a nourishing dietary should be instituted, which, however, limits the nitrogenous articles, and stimulants, such as tea and coffee, are to be interdicted. An outdoor life and frequent bathing are advisable. Schamberg has demonstrated the important influence which diet exerts on the eruptive course of the disease. Such a diet should be low in protein through restriction of milk, bread, and cereals, and avoidance of meat, fish, fowl, and eggs, and the patient must live largely on green vegetables, fruits, and other articles of high caloric value.

Of the internal remedies arsenic is the most constant in its effects, especially when the inflammatory element is not marked. In acute attacks or when the disease is rapidly spreading, arsenic is contraindicated, because it may stimulate the eruption to increased activity. The writer agrees with Ormsby[27] that local treatment should be employed for a reasonable time before resorting to arsenic or other drugs, and that this remedy should be reserved for cases which have resisted other methods of treatment and which are stationary. The preparation in common use is Fowler's solution, which should be given in small, gradually increasing doses, well diluted with water, and always during or after the meal. When prescribing for children, to minimize error in dosage it is well to dilute Fowler's solution with peppermint water (1 :3). Its use should be continued for about one month after the disappearance of the eruption, but it should not be given over indefinite periods for the prevention of recurrences. Arsphenamin is valueless. Salicin is advocated for acute cases, and thyroid extract may be beneficial at times. Injections of autoserum are frequently of value, and should be used before resorting to arsenic.

Successful results in psoriasis depend largely upon local treatment. The first indication is the thorough removal of the scales by the application of oil or vaselin, followed by prolonged alkaline baths with the free use of soap. The preparations of most value for local use are chrysarobin, tar, ammoniated mercury, and salicylic acid, but they must be employed very cautiously with children and only over small areas, to avoid extensive irritation and because of possible toxic effects from absorption.

Chrysarobin is the most effective, but should never be used on the face, hands or scalp because of its irritant and staining properties. Weak preparations should always be tried first, and over a limited surface. A paint with traumaticin (1 per cent.) may be applied every fourth day when the eruption is sparse, a bath preceding each application. When the skin about the lesion becomes red its use should be suspended until the reaction subsides. A sufficiently treated patch will appear white and smooth, while the skin at the periphery is stained purplish-red or brown. Crocker has found chrysarobin valuable in a wide range of cases by using minimal doses of 1, 2 or 3 gr.

to 1 oz. of zinc ointment, but advises its preliminary use over a small area as a test. Chrysarobin should not be used unless the patient is under close medical supervision.

Tar is a valuable remedy and may be used as oil of cade or liquor carbonis detergens (3 to 5 per cent.) in ointments over limited areas. In children with susceptible skins tar readily produces a dermatitis, and when used over large areas may produce toxic effects by absorption. The urine should be carefully controlled.

Ammoniated mercury is a satisfactory application for use on the scalp and face, and on other parts when chrysarobin and tar are contraindicated. It is used in 1 to 2 per cent. strength in vaselin for the face, 2 to 3 per cent. on the body over small areas, and in the same strength on the scalp with the addition of 2 per cent. salicylic acid or liquor carbonis detergens. Toxic effects from absorption are to be guarded against. In children it occasionally produces a violent dermatitis with vesiculation.

Psoriasis patches often respond promptly to treatment with *x*-rays, the use of which should be restricted to those skilled in the technique of its application. This treatment is indicated in circumscribed patches which have proved resistant to other measures.

It is important that treatment be continued with vigor until the last lesion has disappeared, and that for months thereafter a modified form of treatment be followed. This includes attention to diet, daily baths, exercise to promote perspiration, exposure to sunshine, and the rubbing into the sites of predilection of a mild tar and salicylic ointment every second day.

Parapsoriasis.—Parapsoriasis is a term used to designate a group of cutaneous disorders of rare occurrence, closely allied in their clinical and histologic features, which are characterized by persistent, scaling, yellow, pink or red, non-itching macules and patches, and flat papules, usually widely distributed, and refractory to treatment. A number of types have been described under various designations, and these are now generally grouped under the term parapsoriasis, of which three varieties are recognized, the guttate, lichenoid or retiform, and patchy.

Symptoms.—The disorder occurs as a widespread abundant eruption of slow evolution, affecting chiefly the trunk and extremities, rarely the scalp, face, palms and soles, in which the elementary lesion is a small, scaly macule or maculo-papule. New lesions continue to appear gradually, and by peripheral enlargement or coalescence larger lesions are produced, which are usually well defined, superficial, and covered with fine, adherent scales which can be curetted off without bleeding. There is practically no infiltration, except in old patches, and itching is absent. The color of the lesions is pinkish-yellow, red to bluish-red, and of a deeper hue on the legs. The eruption is usually slow in evolution, though in children it has been observed to develop acutely like an exanthem.[28]

In the guttate type the lesions are pinhead to split-pea-sized papules, slightly infiltrated, and covered with a scale which is thicker in the center than at the margin. The eruption resembles an abortive guttate psoriasis, or an involuting papulo-squamous syphiloderm.

In the lichenoid or retiform type the lesions are numerous and coalesce to form a network of extensive distribution which gives the skin a peculiar mottled or marbled appearance. The primary lesion is a yellowish or darker colored, lichenoid papule, covered with scales.

In the third variety of parapsoriasis the lesions are well defined, circular, oval or irregular, non-elevated, slightly infiltrated patches from 1 to 4 in. in diameter, of varying shades of red, yellowish-brown, or fawn color. The patches are smooth or covered with fine, branny, adherent scales, and sometimes are so vague as to resemble fading stains.

In all of its varieties parapsoriasis persists unchanged for years, except for occasional slight remissions or exacerbations. The writer has seen spontaneous disappearance of the disease in a case of the guttate type. The general health is not affected.

Etiology.—The cause is unknown. The disease has been observed as early as the third month of life[29] and frequently develops first during youth and early adult life.

Diagnosis.—The diagnostic features of parapsoriasis are its chronicity, the gradual evolution and persistence of its lesions, their superficial character, the patchy or retiform arrangement, and the general distribution, all of which serve to differentiate it from seborrhoic dermatitis, psoriasis, secondary syphilodermata, pityriasis rosea, lepra, and the premycotic stage of mycosis fungoides.

Pathology.—The histology is that of a superficial inflammatory process in the corium, with dilatation of the capillaries, edema, and lymphocytic infiltration. The changes in the epidermis appear to be secondary and consist of edema, partial or complete absence of the granular layer, and defective cornification, with parakeratosis almost always present.

Treatment.—The disease is refractory to both internal and external treatment. Arsenic in all forms is ineffective. Locally, the applications recommended for psoriasis may be used. It has recently been reported that in all three varieties of the disease the eruption has either been considerably influenced or has disappeared entirely following desquamation produced by exposure to ultra-violet rays.

Herpes Simplex.—**Definition.**—Herpes simplex or "fever blisters" is an acute inflammatory disorder, characterized by the formation of grouped vesicles, closely set or confluent, on an inflammatory base, and attended by a sensation of burning and tension. It occurs in two forms, according to localization: Herpes facialis or febrilis and herpes genitalis.

Symptoms.—The first manifestations are tingling, burning, and a sensation of tension in the affected area, followed by the formation of one or several groups of red papules, which quickly develop into clusters of vesicles upon inflammatory bases. The vesicles are of pinhead to small pea size, and may coalesce to form flat blebs. They contain a clear serum, which later becomes turbid or milky, and only rarely purulent. The vesicles desiccate or rupture, and form yellowish or brownish crusts, which become detached within a few days, leaving red stains and occasionally slightly depressed scars. Swelling of the regional lymph glands is often observed.

In herpes facialis the lesions occur most commonly about the mouth and nose, usually as a single group, although they may appear on any other part of the face except the forehead, and on the neck and ears. In children the eruption is often profuse and may cover a large part of the cheeks, or the lips and chin, and is usually bilateral. The mucosa of the oral cavity, pharynx and larynx may be the site of lesions, which in these locations are often bilateral and recurrent, and attended by mild systemic symptoms. Intact vesicles are rarely seen, as they rapidly become eroded and form painful, superficial ulcers.

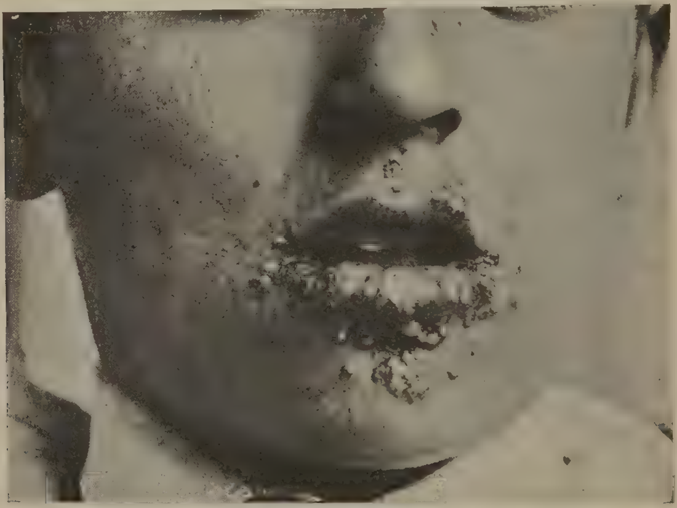

Fig. 44.—Herpes labialis. (Fordyce and MacKee.)

The term herpes genitalis is applied to the vesicular eruption when it affects the genitalia. Clinically it is not essentially different from the disease as it appears in other regions; it is rarely observed in infants or young children.

Numerous instances have been recorded of the occurrence of herpes simplex on the trunk, buttocks, one or several fingers, palm, nipple, and in other situations, either as single clusters or extensive patches of eruption. Although there is a distinct tendency for herpes simplex in any situation to be recurrent, often in the same areas, over a period of years, this is most marked when the eruption affects the face, especially the cheeks, and the fingers in children, and the buttocks, genitalia, and mouth in older subjects. The recurrent forms are often associated with marked burning sensations, neuralgic pains, and some constitutional disturbance.

Etiology.—Herpes simplex appears to be due to irritation or inflammation in the terminal filaments of the peripheral nerves or ganglionic centers, as the result of local irritation, and bacterial, toxic or other systemic agencies. Herpes facialis occurs in a number of acute infectious disorders, and its appearance in epidemic form in children has been described. Lipschuetz[30] and others have succeeded in inoculating the rabbit cornea with herpes simplex, and believe the disease is due to a filtrable virus.

Pathology.—Inflammatory and degenerative changes in the ganglionic centers have been found in herpes facialis occurring with acute infectious diseases. The histopathology is that of an acute inflammatory process with formation of vesicles in the rete.

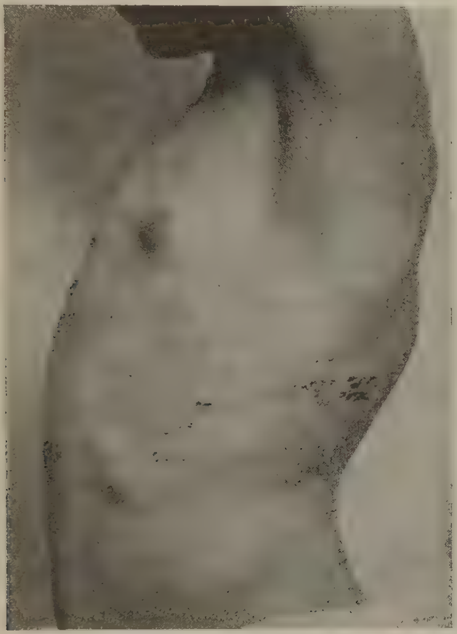

FIG. 45.—Herpes zoster. (Ormsby and Mitchell.)

Diagnosis.—Vesicular eczema and impetigo contagiosa are readily differentiated. In herpes zoster the pain is marked, the lesions are unilateral, often leave scars, and are seldom confined to a limited area such as the lips, and recurrence is rare.

Treatment.—In recurrent cases arsenic and quinin have been advised. Ormsby advocates radiotherapy for both immediate relief and prevention. Applications of spirits of camphor or lotio alba are of service, and will sometimes abort the lesions. Compound tincture of benzoin is a good protective after the vesicles have ruptured.

Herpes Zoster.—Definition.—Herpes zoster is an acute inflammatory, self-limited disease, characterized by the development of grouped vesicles on reddened bases, in the area of distribution of cutaneous nerves, attended by neuralgic pains.

Symptoms.—The eruption may be preceded by systemic disturbance with fever, and by hyperesthesia or neuralgic pain in the affected region. The lesions appear in successive crops, as small erythematous patches or groups of papules, which may not develop further, but which most often rapidly develop into pinhead to pea-sized, tense, thick-walled vesicles grouped upon an inflammatory base. The vesicular patches may be few or numerous, are separated by areas of normal skin, and follow the course of the affected nerve or nerves, the eruption being distinctly unilateral and only rarely bilateral. The vesicles are deeply situated and do not tend to rupture spontaneously. Their contents are clear or turbid, but the vesicles may become pustular or hemorrhagic, and in violently inflammatory cases the lesions may be gangrenous. The regional lymph-glands are enlarged and tender. Within several to 10 days after the onset new lesions cease to develop and the older vesicles dry into yellowish-brown crusts, which, after falling, leave stains or scars. The duration of the disorder

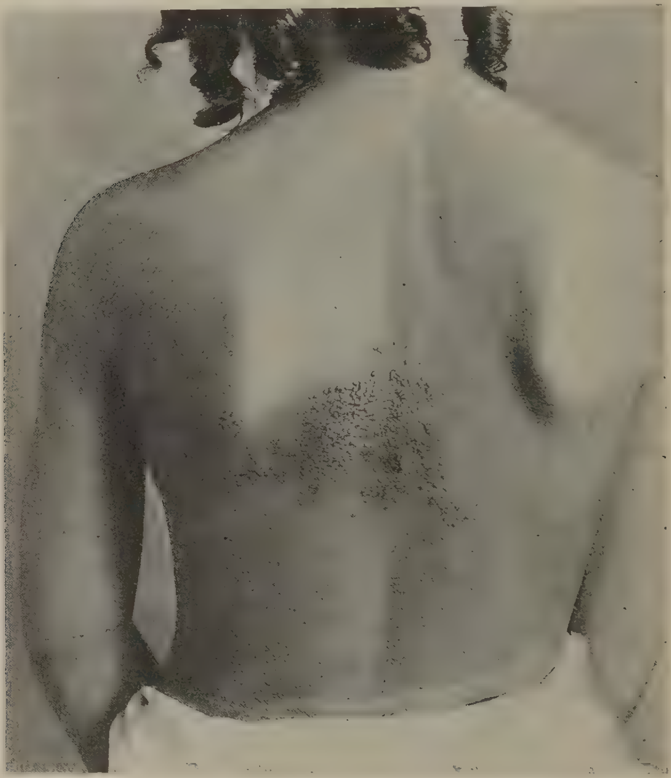
FIG. 46.—Zoster and congenital syphilis. (Fordyce and MacKee.)

is from 10 days to three weeks, and often longer in the gangrenous cases, and a second attack is rare. Pain is a variable symptom; in children it is usually slight or absent, or replaced by itching. The pain is often severe and associated with hyperesthesia, and may continue for weeks after the eruption has disappeared.

The sites of predilection are those supplied by the intercostal, brachial, lumbar, and trifacial nerves, though any region may be involved. In children the intercostal region is most often affected (zoster pectoralis). Herpes zoster ophthalmicus is often a formidable disease with severe neuralgia, and destructive inflammation of the cornea or of the entire eye may occur. In other instances it may pursue a mild course.

The occurrence of a generalized varicella-like eruption in the course of herpes zoster has often been observed[31] and muscular palsy and atrophy may be sequels.

Etiology.—Herpes zoster is most prevalent in the spring and autumn, and occurs at all ages, though it is rare in infancy. Exposure to wet and cold, traumatism, infections, and arsenic are frequent causative factors. It is probable that the disease is an infectious process, not due to a specific microörganism, but to various infections. The work of Rosenow and Oftedal[32] and others indicates that the causative agent may be a streptococcus isolated from the tonsils and pyorrheal pockets, which, when injected into animals, showed an elective affinity for the posterior root ganglia, and produced the symptoms of zoster. The disease occurs at times in epidemics, and in association with other infections such as influenza, malaria, syphilis, varicella[33] and focal infections.

Pathology.—The disease is due to an inflammatory and degenerative process of sensory nerve structure, most frequent in the ganglionic centers, or in the posterior roots, or occurring as a descending neuritis, or as a peripheral neuritis without involvement of the ganglia. The cutaneous changes involve the epidermis and corium. The vesicles are deeply seated, usually unilocular, intercellular, and involve the lower rete or lie between the epidermis and corium. In the papillary layer of the corium there is edema, vascular dilatation, and leukocytic infiltration, and, in severe cases, necrosis with destruction of the papillæ.

Diagnosis.—The clinical picture presented by herpes zoster is distinctive and the disease can usually be recognized without difficulty. Abortive or mild forms of zoster may be confused with herpes simplex, but the latter is often recurrent, bilateral, and unaccompanied by pain.

Treatment.—The treatment is symptomatic and palliative. Severe types require rest in bed and the use of anodynes. Acetyl salicylic acid and phenacetin are useful if the pain is moderate. The unruptured lesions should be covered with a dusting powder of equal parts of starch, boric acid and talcum powder, and protected by a dressing of absorbent cotton, or when the lesions are not extensive they may be painted with a 12 per cent. ichthyol-collodion mixture.

When the lesions have ruptured compresses of boric acid solution are to be used for drainage, alternating with a carbolized zinc oil. Ointments are often not well tolerated in the early stages, though mild antiseptic ointments are of service later or if secondary infection has occurred. If the pain is severe or persistent, which is unusual in children, a mild galvanic current applied in the course of the nerve often gives relief.

Pompholyx.—Definition.—Pompholyx or dysidrosis is an acute inflammatory affection of the hands and feet, characterized by deep-seated, firm vesicles and bullæ.

Symptoms.—The disease begins with sensations of burning or itching, followed in a few hours by the rapid development, on the hands and feet, of small, deep-seated, tense vesicles, resembling boiled sago grains. The vesicles are usually closely aggregated and remain discrete or coalesce to form pea-size or larger bullæ. The lesions occur singly and in small groups, or may be numerous and cover the entire part. The eruption is often symmetrical and usually affects the palms and the palmar and lateral surfaces of the fingers. The dorsum of the hands and the plantar surfaces of the feet are less often involved. The lesions on the palms and soles do not tend to rupture spontaneously, and usually disappear by absorption, with exfoliation of the epidermis, leaving a reddened surface. When the skin is thin the larger lesions may rupture and expose a tender, inflammatory, moist base, sometimes covered with a grayish, necrotic pellicle. In severe forms the affected parts are tense, swollen and painful, and if secondary pus infection occurs the inflammatory process may become extensive and complicated by lymphangitis. The individual lesions disappear in one or two weeks, but new lesions may continue to appear and prolong the course of the disease for weeks. Recurrences are common, especially in the warm months and after exposure to heat.

Etiology.—Pompholyx may occur at any age, and is common in children and rare in infancy. Hyperidrosis may be an associated condition, but it is often absent. It is generally regarded as a vasomotor neurosis. In the past few years, in a large proportion of cases of pompholyx, microscopic examination has disclosed the presence of a ringworm fungus, the *Epidermophyton inguinale*, and it is probable that many of the cases recorded as pompholyx or dysidrosis are vesicular and bullous types of ringworm.[34] Darier and Jadassohn do not consider pompholyx an entity, an opinion which is shared by many dermatologists.

Pathology.—The original investigators of the histopathology of pompholyx believed that the lesions were in anatomic relation with the sweat gland ducts, but later studies by Robinson, Sutton and others do not show this connection, the vesicles being found in the supra-papillary portions of the rete.

Diagnosis.—Artificial eczema or dermatitis due to local irritants, and the vesicular forms of epidermophytosis may present the clinical picture of pompholyx, and the differentiation is made on the basis of etiology. A recurrent desquamation of the hands and feet is often observed in warm weather in individuals with an ichthyotic type of skin, in which the epidermis is raised and exfoliates at numerous points, often forming small polycyclic patches, without inflammatory changes. This is a physiologic process, and the absence of vesiculation readily differentiates it from pompholyx. Eczema of the palms is erythematous in type, and eczema on other parts of the hands and on the feet presents primarily an itching, superficial, papulo-vesicle, which ruptures readily and weeps. Pompholyx is to be differentiated from an inflammatory eruption of closely set, uniformly pinhead-size vesico-papules or vesicles covering the palmar and plantar surfaces which sometimes occurs as a manifestation of a toxic condition. In contrast to pompholyx it appears suddenly and usually subsides within a few days without exfoliation, and fungi are absent.

Treatment.—In cases in which a local irritant or infective cause is not demonstrable, the general health may require attention. Good hygiene and tonic medication, with particular reference to a defective peripheral circulation, are important. Locally, the calamin lotion, diluted black wash, or lead water and boric acid solution are useful used alone or combined with soothing ointments. Zinc paste with 2 per cent. salicylic acid, applied under a bandage, is an excellent preparation. If fungi are found the treatment is that described under ringworm of the extremities.

Pemphigus.—**Definition.**—Pemphigus is an acute or chronic disease of the skin characterized by the rapid development of bullæ, often on apparently normal skin, accompanied by constitutional symptoms of varying degree. It is a rare disorder, and occurs in four clinical varieties: Pemphigus acutus, pemphigus vulgaris, pemphigus foliaceus, and pemphigus vegetans.

Pemphigus acutus occurs in connection with septic wounds and vaccination,[35] runs a rapid course, with severe systemic symptoms, and is often fatal. The bullous eruption is generally widespread, often hemorrhagic, and tends to involve the mucous membranes. The disease is an expression of a general sepsis, and its inclusion in the group of true pemphigus is open to question. It should not be confused with an acute bullous eruption of infants, so-called pemphigus neonatorum, which often occurs in epidemics in institutions. This is due to local infection with pus organisms, and is a bullous form of impetigo contagiosa.[36]

Pemphigus vulgaris or chronicus is the most common form of pemphigus, and though occurring most often after the age of 40 is not infrequent in children. Mild or severe systemic symptoms often precede or accompany the appearance of the lesions, which develop rapidly upon normal or slightly reddened skin, as few or numerous, isolated, tense or flaccid, hemispherical or oval bullæ, varying in size from that of a pea to an orange. They rise abruptly from the skin, are distended with serous, sero-purulent or hemorrhagic fluid, and do not tend to enlarge but multiply in crops or in continuous succession, and often coalesce. New bullæ may form repeatedly upon the same spot. Zeisler has observed that the bullæ are tense in the milder cases and flaccid in the serious ones. Unless accidentally ruptured, the bullæ persist for a week or two, the contents disappear by absorption, the affected area exfoliates, and a violaceous, thinned epidermis remains, which later is pigmented. Ruptured lesions form crusts, overlying a smooth, inflammatory, often suppurating surface, and a horny epidermis develops. In serious cases the eroded areas are slow to heal, the edges are loosened by exudate, neighboring lesions tend to coalesce, and polycyclic, denuded and crusted areas of considerable extent are formed, with continual breaking down of the newly formed epidermis.

The lesions may appear anywhere, but the parts usually affected are the extremities, face, and trunk, and especially the cutaneous folds. The mucous membranes of the mouth, nares, lips and vagina may be involved, and sometimes are primarily affected, in which event the prognosis is especially grave.

The disease may run an acute and rapidly fatal course, or may be mild in type and end in recovery after several months. The less severe forms, which occur especially in children, may end in recovery after repeated relapses. In most cases the course is slow, new lesions recur at intervals for months or years, the general health is impaired, and death results from exhaustion or some intercurrent disease.

Pemphigus foliaceus may develop from pemphigus vulgaris and other dermatoses or as a primary disorder. The lesions are flaccid bullæ, which rupture and form crusts, and when these are cast off a denuded surface remains, upon which new bullæ continue to form. The disease often becomes universal, the mucous membranes are involved, and after a few months, or rarely years, the patient succumbs. A characteristic feature of this variety of pemphigus is Nikolsky's sign, which is produced by slight lateral pressure with the finger, thereby causing a separation of the upper layers of the epidermis, which is saturated with serum, from the deeper parts.

In *pemphigus vegetans* papillomatous or vegetative masses develop upon the sites of ruptured bullæ. The disease often begins with bullæ on the mucous membranes, soon followed by lesions which develop vegetations and are usually found in the ano-genital region, neck, axillæ, flexures, and scalp. Periods of partial remission may occur and delay the ultimate fatal outcome for months, or the disease may be rapidly fatal.

Etiology.—The cause of pemphigus is unknown. It is a rare disease, and occurs in both sexes and at any age, and is relatively frequent in children. Pemphigus foliaceus and vegetans are extremely rare forms. It is not contagious and heredity is not a factor, though the Jewish race appears to be predisposed to it. In the opinion of many observers the disease is due to the action of various toxic agents on the nervous system; other observers contend that it is microbic in origin.

Pathology.—The bullæ are developed beneath the stratum corneum at various depths in the rete mucosum and are epidermal, though exceptionally they may form beneath the epidermis with the papillæ as the base. The papillary and subpapillary vessels are dilated, there is perivascular serous exudation, and round-cell infiltration in the corium. The contents of the bullæ consist of serum, disintegrating leukocytes, eosinophils, and cell debris. In pemphigus vegetans the papillæ are hypertrophied and the lymph vessels are widely dilated.

Diagnosis.—The essential features of pemphigus are sufficiently characteristic to prevent confusion with disorders in which bullæ sometimes occur, such as urticaria, pompholyx, erysipelas, epidermolysis bullosa, scabies, and bullous drug eruptions, which in addition to bullæ exhibit other associated symptoms. The bullous syphiloderm occurs in infants with hereditary syphilis, and is usually confined to the palms and soles. When the primary bullæ of pemphigus appear on the mucous membranes of the mouth they may readily be mistaken for syphilitic lesions, but the subsequent course and the absence of other evidence of syphilis establishes the diagnosis. Bullous impetigo of infants, so-called pemphigus neonatorum, and that seen in older children, is contagious, auto-inoculable, and in addition to bullæ often presents typical lesions of impetigo contagiosa. Bullous lesions in erythema multiforme arise from an erythematous base, are usually limited in number, confined to the sites of predilection for this disease, and are associated with other characteristic lesions of erythema multiforme. The differentiation of pemphigus from dermatitis herpetiformis may be difficult and sometimes impossible. In dermatitis herpetiformis the itching is usually intense, the lesions are multiform, erythematous patches, papules, vesicles and pustules being present at some time during the eruptive periods, and there is a marked tendency to grouping, although in children itching and grouping are not as prominent features as in the adult.

Prognosis.—The prognosis in pemphigus is always grave. Mild cases, particularly in children, may recover. Relapses are frequent and the disease may extend over a period of years before death occurs. The severe cases of pemphigus vulgaris, and the foliaceus and vegetating forms, are invariably fatal. Involvement of the mucous membranes and of extensive areas of the skin, repeated outbreaks, flaccid lesions with purulent or hemorrhagic contents, and marked systemic disturbance are unfavorable indications.

Treatment.—There is no specific remedy for the treatment of pemphigus. Arsenic is of value in some cases, and others are temporarily benefited by quinin given intravenously. Arsphenamin has been used in some cases with apparently good effects, but in the writer's experience, which agrees with that of Ormsby, it has not been of value. Autogenous vaccins and auto-serum injections have likewise proved useless. The general management of the patient and the maintenance of a good state of nutrition are of great importance. Much can be accomplished by good hygiene, a nutritious diet, daily baths, and tonic medication with iron, malt, and cod-liver oil. Adamson[37] states that in the case of children confinement to bed and daily baths are of decided value, though relapse often occurs if the patient is allowed to get up too soon. In severe or extensive cases the patient should lie on an air or water mattress, and a continuous water-bath may be used for several hours daily unless it proves exhausting.

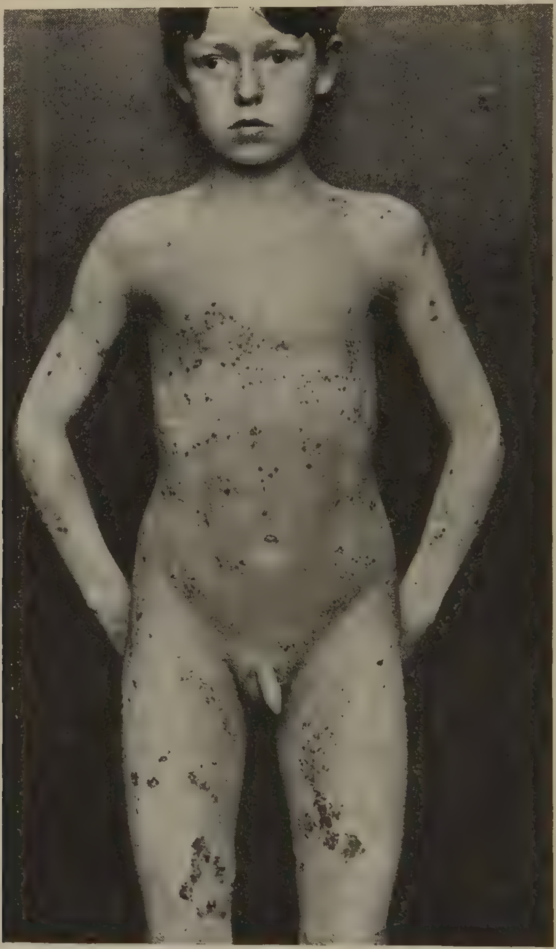

Fig. 47.—Dermatitis herpetiformis. Chronic. Erythemato-vesicular variety. (Collection of Dr. Grover W. Wende.)

Local treatment aims to promote healing, prevent infection, and relieve the subjective symptoms. Bullæ should be punctured at their bases and evacuated, and dressed with gauze dipped in olive oil and lime-water, or with calamin emulsion, to which 1 per cent. of carbolic acid may be added. Similar dressings may be used for the denuded surfaces, or bland ointments such as zinc oxid or boric acid ointment may be more comforting. In some cases liberal applications of powder, such as magnesium carbonate, boric acid and talc, are more effective than ointments, but crust formation must be avoided It is important to maintain drainage and prevent absorption of decomposing epithelial products and secretions, and for this purpose colloid or sulphur baths are most useful, especially in cases with extensive lesions and in pemphigus foliaceus. Careful nursing and the skillful, rapid application of local remedies and dressings are of great importance in the management of all cases of pemphigus.

Dermatitis Herpetiformis.—**Definition.**—Dermatitis herpetiformis is a chronic, relapsing inflammatory disease, characterized by a multiform eruption of erythematous, papular, vesicular, bullous or pustular lesions, which tend to form groups, often appear in certain sites by preference, and are usually attended by marked itching and burning.

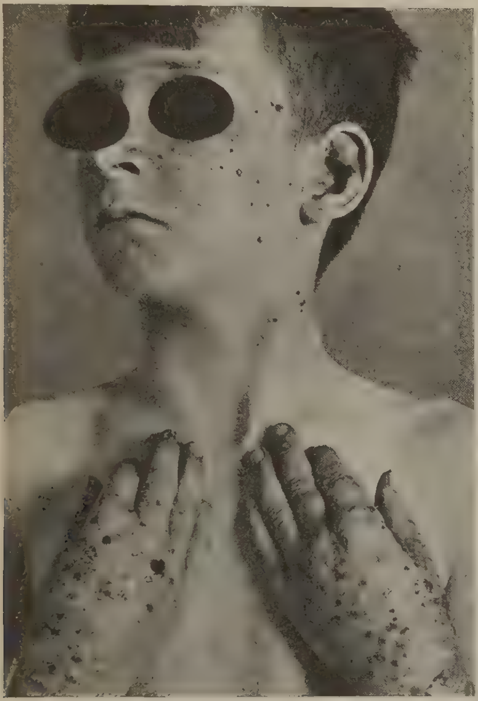

Fig. 48.—Dermatitis herpetiformis. (Fordyce and MacKee.)

Symptoms.—The eruption appears gradually or suddenly, with or without mild constitutional symptoms, and in its development is attended, as a rule, by intense itching or burning sensations. The distribution is fairly symmetrical, and in cases of long standing a distinct preference is shown for the scapular, sacral and trochanteric regions, and the extensor surfaces about the elbows and knees. The eruption may be predominantly erythematous, papular, vesicular, pustular, or bullous, or it may be multiform or mixed, and retain its uniformity of type during relapses, or the type of eruption may undergo change at any time. The vesicular is the most characteristic form, and with the multiform variety represents the disease as it is most commonly observed. The lesions tend to appear in successive crops at irregular intervals, with periods of complete remission followed by recurrence, for a period of months or years. In the course of time most of the cutaneous surface may have been affected, as shown by extensive pigmentary remains. A frequent feature is the arrangement of lesions in clusters or groups and rings with peripheral spreading. Pigmentation of varying degree is present in all cases and may be intense. As a result of secondary infection following scratching, the regional glands may be enlarged and tender, and the skin may become thickened and lichenified from trauma.

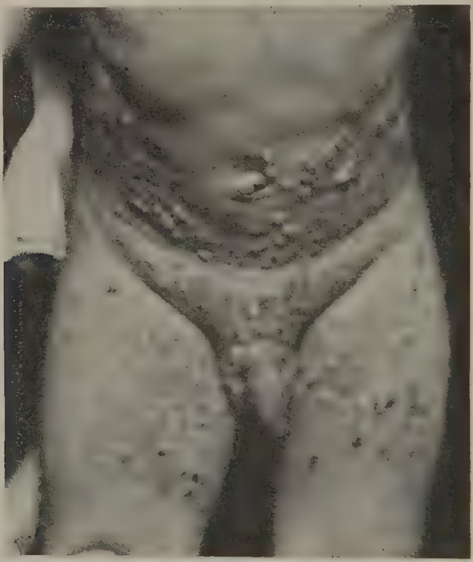

Fig. 49.—Dermatitis herpetiformis bullosa in a child of 6 months. (Bowen.)

The erythematous variety occurs in reddened, diffuse or marginated, often urticaria-like patches of coin to palm size, associated with intense burning and itching. Maculo-papules and papulovesicles often co-exist. In the vesicular type the lesions are miliary to pea-sized, angular or stellate, flat or elevated, tense, firm walled, pearly vesicles, which appear in crops. They may be widely separated, but usually occur in clusters, composed of several discrete vesicles, or in larger groups of closely set, coalescing vesicles of varying size which form irregular bullæ. The itching and burning is often intense, and is usually relieved by rupture of the lesions. The pustular type occurs with pinpoint to pinhead-sized, flat lesions, or as large, elevated, rounded pustules with an inflammatory areola, which desiccate and form brownish adherent crusts. This variety tends to remain pustular throughout its course and is usually attended by more systemic disturbance than is present in other forms.

Lesions may appear on the mucous membranes of the mouth and nose, and rarely on the conjunctiva, and form painful erosions covered with a necrotic membrane.

The course of the disease is chronic, more or less extensive exacerbations and relapses alternating with periods of relative inactivity. The general health is usually unaffected, though as a result of intense itching and disturbed sleep many patients are nervous, depressed, and physically reduced.

Dermatitis herpetiformis in childhood differs from the disease as observed in adults in several important particulars. Knowles' study[38] of the literature in this connection shows that in children the most common type of eruption is the vesico-bullous, with the multiform type next in frequency, and the papulo-vesicular or the pustular as infrequent varieties. The distribution is general, the face and extremities being chiefly involved, with the lesions often appearing first on the legs. Grouping of the lesions, itching, and pigmentation are not as frequent nor as characteristic as in adults, and may be lacking. The disease has been observed repeatedly in early infancy, though it most commonly affects children between the ages of 6 and 10, the majority of cases being in males.

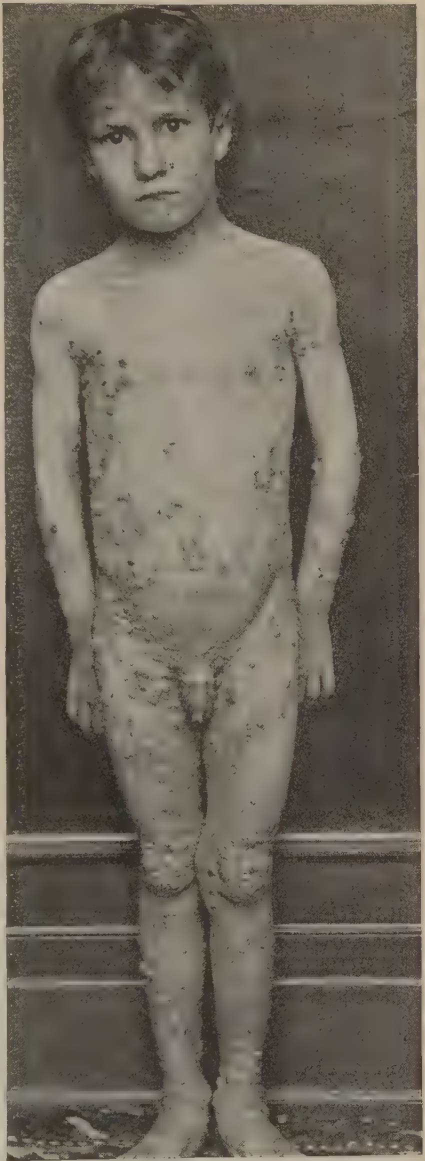

FIG. 50.—Dermatitis herpetiformis bullosum—bullous eruption. (Collection of Dr. Grover W. Wende.)

Etiology.—The cause of dermatitis herpetiformis is unknown. It has followed vaccination, infections, and nervous shock, and has been brought into relation with tooth and tonsillar infection. Hartzell[39] states that the disease is due to a toxemia of undetermined origin, and MacLeod[40] ascribes as causative a non-specific autogenous toxin, called forth by a variety of influences, which most probably acts indirectly on the skin through the nervous system.

Pathology.—There is an acute inflammation of the upper corium, chiefly in the papillary layer, with vesicle formation between the lower rete and the papillary body. The epidermis shows edema, and there are few changes in the lower corium. Eosinophil cells are found in the vesicles and in the lymph spaces and vessels of the corium. Eosinophilia is often present, especially in the cases occurring in children.

Diagnosis.—Cases presenting the characteristic features of multiformity and grouping of lesions, intense itching, chronicity and repeated recurrences are readily recognized. In exceptional instances the differentiation between pemphigus vulgaris, erythema multiforme, and dermatitis herpetiformis may prove to be very difficult or even impossible. In pemphigus vulgaris the lesions are thin-walled, usually large bullæ arising rapidly from apparently sound skin, without tendency to symmetry in distribution, the mucous membranes are often involved, and itching is slight or absent. In erythema multiforme the eruption shows a predilection for certain sites, the bullæ develop secondarily and are associated with other characteristic lesions of the disease. The papular variety of dermatitis herpetiformis when of long standing may resemble prurigo, but the eruption is rarely as extensive or continuous, the infiltration and lichenification are less marked, the adenopathy is not as pronounced, and vesicles are present at some time in the course of the disease.

Prognosis.—The disease may be mild and of short duration, but more often it is persistent and recurrences prolong its course indefinitely. The bullous and pustular forms are more serious than the other varieties, and may terminate fatally. The prognosis is more favorable in children than in adults.

Treatment.—The general condition of the patient should receive careful attention, with especial reference to elimination, nutrition, rest, and general hygiene. A vegetarian diet is sometimes of benefit. Cod-liver oil, calomel, salol, alkalis, and diuretics may be used as indicated. Quinin and nux vomica are useful tonics. In most cases, and especially in children, the eruption is mitigated or controlled by arsenic, though it does not prevent recurrences. It is given as Fowler's solution in gradually increasing dosage until the lesions are influenced, or to the physiologic limit if necessary, and the effective dosage is maintained until the lesions have disappeared, and is then gradually reduced. Arsenic should not be continued for a longer period nor in larger dose than necessary, in order to avoid gastric irritation and the production of hyperkeratoses and hyperpigmentation. Auto-serum injections given repeatedly exert a marked beneficial effect on the eruption and on the course of the disease in some patients, while in others they are ineffective. Adrenalin, thyroid extract, antipyrin and arsphenamin have been advocated, but the results are uncertain.

Itching is relieved by puncture of the vesicles, combined with the use of lotions containing 0.5 to 2 per cent. of phenol and 5 to 20 per cent. of liquor carbonis detergens (Wright's). A carbolized zinc oil or an ointment of phenol, menthol, salicylic acid and naftalan is useful in cases with excoriated lesions. Baths containing sulphur (Vleminckx's solution or potassium sulphid, 1 to 2 oz. to 15 gal. of water), bran, starch or oatmeal are of considerable value in extensive and very pruritic cases, and the effect is prolonged by liberal applications of a camphorated dusting powder after the skin has been allowed to dry without rubbing.

Eczema.—Eczema is an acute, subacute or chronic inflammation of the skin, characterized by erythema, papules, vesicles or pustules as primary elements, with secondary changes resulting in exudation and crusting, or infiltration and scaling, and attended by sensations of itching and burning.

Although eczema is protean in its clinical manifestations and varied in its causation, the various forms in which it appears possess essential features in common which indicate a pathologic unity.

Symptoms.—Eczema begins with erythema in patches, with papules, vesicles, or pustules, or as a mixture of two or more of these types of lesions, which develop in one or several limited areas in groups or patches of varying size, or as a more widely diffused or generalized eruption of discrete or grouped and patchy lesions, often bilateral and symmetrical in distribution. Any part of the cutaneous surface may be involved, but the eruption shows a predilection for the flexor surfaces and for the hands and face. New lesions make their appearance irregularly or in crops, and the eruption extends gradually or rapidly by involvement of the neighboring surfaces or by the development of lesions in new areas. Unless an eczema is acute in type clinically and ends in several weeks, which is exceptional, its further course is marked by frequent changes in the severity of the process and is subject to remission and exacerbation at irregular intervals. Secondary inflammatory changes become more pronounced and the disease gradually assumes a chronic type and course, with acute and subacute exacerbations, and continues indefinitely.

While the eruption of eczema is primarily erythematous, papular, vesicular, or pustular, this uniformity of type is not retained for any length of time, except in the erythematous and less often the papular varieties. Lesions of another type soon develop or the eruption is multiform from the beginning, although, as a rule, in mixed forms of eczema one type of lesion predominates and new lesions conform to this type. Secondary or consecutive forms are also evolved from the primary types, and are characterized by exudation, crusting, infiltration, and scaling. Moreover, eczema possesses certain features which may be regarded as essential, all or most of which are present at some time in every case. These are redness, infiltration varying in degree from slight in the acute forms to marked in the chronic types, some scaling or crusting, itching and burning of variable intensity, and a serous exudation or discharge.

Erythematous eczema occurs most often on the face, genitalia, in the flexures, and on opposed surfaces in diffuse or localized patches of erythema which tend to coalesce, are slightly scaly, edematous in the acute forms and infiltrated in subacute and chronic cases, and is accompanied by itching and burning sensations. It is often converted into the vesicular, pustular or squamous type, tends to recur, and often becomes chronic.

Papular eczema is characterized by the presence of rounded or acuminate, pinhead-sized or larger, red or bluish-red papules, often capped by minute vesicles. They may be discrete or closely aggregated, and may coalesce to form infiltrated scaly patches. The papules occur in small groups, forming coin-sized or larger, irregular, elevated patches with discrete lesions scattered about the periphery, and involving the trunk, face and extremities, or the papules are discrete and widely distributed, affecting especially the back and the extensor surfaces of the arms and thighs. The itching is usually intense, and as a result of scratching the papules become abraded and ooze serum, or are lacerated and covered with blood-crusts. Long continued rubbing may transform the papules into glazed, flattened and angular lesions resembling those of lichen planus. Papular eczema is resistant to treatment, exacerbations and relapses are frequent, and it tends to persist.

Vesicular eczema usually begins acutely with swollen, intensely reddened patches upon which numerous, pinpoint to pinhead-sized, acuminate or rounded vesicles rapidly develop. The vesicles are discrete or more often closely crowded and confluent, rupture readily and exude a clear, sticky serum, which dries into yellow, varnish-like crusts beneath which exudation continues. Large or small, weeping, deep red, partly crusted, infiltrated patches are produced, with indefinite borders fading gradually into the normal skin (eczema rubrum or madidans). As the intensity of the process diminishes the redness fades, edema and infiltration decrease, the exudation subsides, scaling occurs and a new epithelial covering is formed. Vesicular eczema may remain confined to one or several small areas, as on the hands and feet, the lesions appearing at irregular intervals and developing more or less symmetrically in small groups, or it may occur over extensive areas in large confluent patches, and is rarely generalized. It may occur anywhere on the skin, including the scalp, but is most commonly seen upon the face in infants and young children, on the flexor surfaces, especially near the joints, on the neck and scrotum, and where the skin is thin. This variety may be acute and end in a few weeks, but its course usually is chronic with frequent exacerbations, and the usual termination is in eczema rubrum or, less often, in squamous eczema. Itching and burning are often pronounced.

Pustular eczema may develop from another form, usually the vesicular, as a result of secondary pus infection, or it may begin with pustules. These are small, acuminate lesions situated on an inflammatory base, which rupture readily and form yellowish-green or brownish friable crusts, overlying a denuded surface which exudes a mixture of serum and pus. Many cases of this variety are instances of infectious eczematoid dermatitis as described by Engman and Fordyce. The parts commonly affected are the scalp and face, especially in children, and it may appear on the legs as a follicular eruption in which superficial pustules develop about the hair follicles. Pustular eczema is seen most often in poorly nourished and debilitated subjects, usually children, and pursues a chronic course with exacerbations.

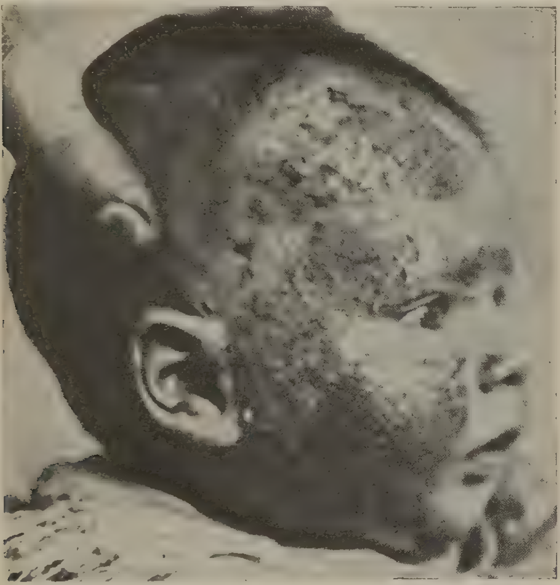

Fig. 51.—Eczema infantile. (Fordyce and MacKee.)

The four primary types undergo consecutive changes and modifications, varying according to the intensity or some peculiarity of the inflammatory process, the influence of various external and internal factors, the region affected, and various other conditions, which result in the production of an infinite variety of clinical pictures, in all of which, however, the essential features of eczema may be recognized. Among such secondary or modified types are included squamous, fissured, verrucose, sclerous, tylotic and nummular eczema, and the topical varieties which often present certain characteristic features in their special locations.

Eczema in Infants and Children.—The description of eczema given on the preceding pages, though general in its scope, provides a basis for the further and more detailed consideration of the condition as it occurs in infants and children. Eczema in early life presents certain features, aside from those related to causation, which may be considered as distinctive although it does not differ essentially from the disorder as it occurs in adults. The same primary types are encountered, though usually in a more acute and inflammatory form, and they are often accompanied by systemic disturbance. There is a marked tendency to involve the face and scalp, and in the large majority of cases the eczema has its origin in these locations. The course, though chronic as to duration, is often an almost continuous train of acute symptoms, and the moist and squamous types are frequently seen. Infiltration and thickening are usually not pronounced in children, even in the chronic types. The superficial lymph-glands are often enlarged and tender, especially in the post-cervical region, but suppuration is uncommon.

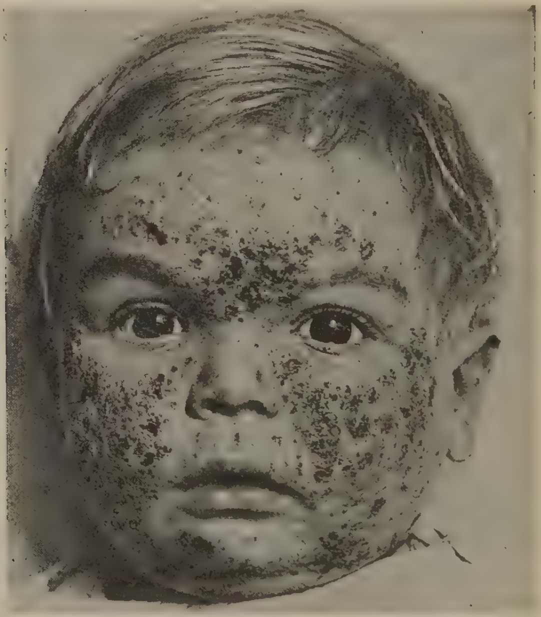

Fig. 52.—Eczema infantile. (Ormsby and Mitchell.)

Infantile eczema generally begins on the face, often over the flush area of the cheeks, or on the scalp, less often on the hands and arms, and exceptionally on other parts. It may appear in a mild form, often limited to one or both cheeks, and consist of one or several illy defined, slightly scaly erythematous patches on which a number of papules or papulo-vesicles may develop. The erythema subsides and is succeeded by scaling patches, or more commonly, the inflammatory process increases in intensity, or is intense from the beginning, and numerous small, bright red papules develop, which are rapidly converted into vesicles. These coalesce and more or less edematous, weeping patches are formed, surrounded by an erythematous zone, in and beyond which discrete papular and papulo-vesicular lesions are scattered. The eruption may now become puriform, or it may be pustular almost from the beginning, and yellowish or dark colored crusts are formed. At its acme the process is one of acute dermatitis The skin is swollen and its surface is intensely reddened, granular, bleeds readily, and exudes a serous or sero-purulent fluid in profusion. The secretion dries and forms thin, varnish-like or gummy crusts, often spread over the affected surface as an almost continuous uneven contractile sheet, traversed by irregular, crack-like fissures and by excoriations due to scratching, which bleed or exude a sero-pus. When pus formation is abundant the crusts which form are thick and heavy, dirty-yellow or dark in color, and cover a large portion of the affected surface. The exudative condition is usually maintained over a long period, with rapid and frequent variations in its intensity, and then gradually assumes the character of an eczema rubrum, or it subsides into the squamous form of eczema. The course is usually irregular and protracted as a consequence of repeated exacerbations and relapses with return to the acute stage, and the disease may last for months or years.

The mild forms of infantile eczema are apt to be confined to the cheeks or to the cheeks and forehead; these areas may also be intensely affected for long periods in certain cases without the appearance of a single lesion on other parts. However, if the process is sufficiently intense to produce vesiculation, or if it is pustular, the eruption is usually more widespread, and in addition to the face it involves the scalp, the retro-auricular region and the neck, often in a confluent series of patches.

Coincident with or shortly after the appearance of the disease on the face, it commonly develops on other parts, especially about the wrists, on the outer side of the legs, the sides of the trunk, over the buttocks and lumbo-sacral region, and in the inguinal folds, usually as a scattered or patchy eruption of small, discrete inflammatory papules or papulo-vesicles, which sometimes exhibit an urticarial tendency. The eruption in these areas varies in intensity, periods of almost complete subsidence alternating with violent exacerbations, during which the process may invade new areas and even become generalized.

Eczema in nurslings, when developing on a seborrhoic basis, usually begins as an erythema advancing from beneath the seborrhoic accumulations present on the scalp. Shortly afterward numerous small red papules, scaling, red, small coin-sized macules, and larger, slightly infiltrated, scaling patches appear on the face and other parts, the eruption extending later from the inguinal folds and buttocks over the abdomen and legs in bright red, erythematous sheets bordered with gyrate, scaling patches. This type of eruption (eczema seborrhoicum) may involve almost the entire cutaneous surface and is distinguished by the smooth, satiny, deep red erythema, and the granular, greasy character of its scales. In its severe form it is indistinguishable from the desquamative erythrodermia of Leiner.[51]

In older infants eczema of the face and scalp on a seborrhoic basis is usually confined to those regions, though other parts may show a few scattered lesions. The scalp is especially involved, and is diffusely covered with a thick mass of yellow, greasy crusts, often extending downward on the forehead and to the ears, from beneath which the seborrhoic dermatitis progresses over the cheeks and lower part of the face.

In older children eczema tends to involve the extremities, especially at the flexures, and the genital regions, and is usually limited in its distribution. Its usual form is that of a pruriginous, dry, scaling, papular eruption with infiltration, or it may occur in erythemato-squamous patches in one or several locations. The generalized or widespread, papular, infiltrated and lichenified type is most often a continuation or relapse of the disorder originating during infancy. In many of these chronic forms of eczema the patients possess xerotic or ichthyotic skins, which modifies the clinical picture considerably and leads to aggravation in cold weather.

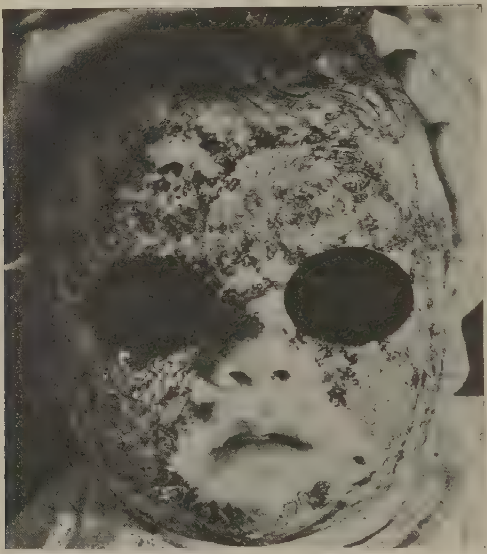

Fig. 53.—Eczema. (Fordyce and MacKee.)

The invasion of the weeping eczematous skin by pus cocci results in increased exudation and the formation of thick, bloody and purulent crusts (impetiginous eczema). Less often pyogenic infection is manifested by the development in the eczematous area of numerous superficial, discrete pustules which may suddenly spread over a large extent of the cutaneous surface, frequently accompanied by febrile symptoms. These pyodermias not only further increase the sensitiveness of the diseased skin and thereby favor the spread of the eczematous process, but they may induce septic complications such as osteomyelitis, furunculosis, perinephritic abscess, endocarditis, and nephritis.[51] The presence of a crusted and pustular dermatitis most marked in the suboccipital region is often evidence of an associated pediculosis.

Itching is usually a prominent symptom. It may be periodic or continuous, is often intense, and causes violent scratching or rubbing if the patient is not forcibly controlled. Restlessness and loss of sleep may impair the general health, but in most patients this remains uninfluenced. Constitutional symptoms consist of mild febrile disturbances at the beginning of the disease or during acute exacerbations, and if pronounced are usually referable to a complicating process. Infectious diseases and acute gastro-intestinal disorders may have a marked effect on the eczematous eruption, and frequently cause its temporary disappearance, and sudden loss of weight in infants is often followed by subsidence of the eruption.

The association of bronchial asthma and eczema is often observed, one disorder alternating with the other at irregular intervals, a condition which Walker[41] and others have shown to be due to protein sensitization in many instances. Engman has demonstrated the relationship of certain types of eczema to hypothyroidism.

Etiology.—Eczema has diverse causes, both local and internal, though in the eczema of early life local irritants are in general less prominent as causative factors than in the eczema of adults. It is a matter of common observation that in many instances irritation of the delicate skin of children by cold, soap, dirt, maceration, friction, decomposition products of the cutaneous secretions, medicinal and other applications is responsible for the development of an eczematous process. But the action of such external factors must be further supplemented by an individual predisposition, for, under the same conditions of local irritation, not all but only a small minority of children will develop eczema. At present our knowledge concerning the nature of the predisposition is fragmentary, though it appears to be definitely established that cutaneous sensitization plays a prominent rôle. Errors of metabolism are also of importance, and a close relation exists between eczema and overfeeding, underfeeding, and various digestive disturbances, and in some instances faulty action of the internal secretory glands apparently underlies the predisposition. The exudative diathesis of Czerny is regarded by some excellent authorities as expressive of the basic tendency which responds to an exciting agent with the production of an eczema. Similarly, the French look upon eczema as a symptom of the "arthritic diathesis."

As in urticaria, a direct influence of diet is often evident. Towle and Talbot[42] found a frequent association of indigestion of fats and carbohydrates in the acute exudative types of eczema in children under two years of age. White[43] in an investigation of the stools of eczematous infants found an excess of fat in those of children with moist types of eczema and an excess of starch in the dry types. The mineral matter of the diet has been held responsible by Finkelstein and his co-workers.

Recent investigations of the proteins by Blackfan, Schloss, O'Keefe, Walker, Engman, and others have shown a high percentage of protein sensitization in infantile eczema by the cutaneous sensitization test, which is significant when contrasted with a negligible incidence of protein sensitization in normal children reported by Baker.[44] A positive response is obtained most frequently to egg, cow's milk, breast milk, wheat, potato and oat. The child may be sensitive to one or more proteins, including foreign proteins obtained through breast milk, and Schloss states that the food allergy may be cyclic, which indicates the need for repeated tests. Crozer Griffith is of the belief that other food substances than proteins can produce eczema. O'Keefe[45] from a study of protein sensitization in eczema in infants and older children concludes that faulty digestion of protein, with consequent absorption in an undigested state, is the most striking common feature of these cases of eczema.

Eczema is not in itself hereditary, and dentition and reflex irritation do not cause the disease although they may aggravate it. Vaccination does not induce eczema and any connection between the two is accidental. Seborrhea of the scalp is frequently associated with eczema, and the irritation produced by the efforts to remove the seborrhoic scales and crusts frequently initiates a dermatitis. It is generally held that eczema is not due to the action of a specific microörganism, though some observers claim that bacterial toxins are concerned in its production. However, staphylococci and streptococci as secondary invaders often have an important influence on the evolution of the lesions.

Pathology.—The pathologic changes involve both epidermis and corium, and vary with the type. In acute eczema the epidermis is edematous, and vesicles are formed at different levels, usually in the upper rete by an interstitial and parenchymatous edema. The rete hypertrophies (acanthosis) and imperfect cornification (parakeratosis) results in scaling. The corium shows vascular dilatation, edema, and cellular infiltration, most marked in the papillary layer. If the disease persists the entire corium is involved, down to the subcutaneous layer. In eczema rubrum or madidans the stratum corneum is cast off without vesiculation, and the edematous rete is directly exposed and exudes a characteristic syrupy fluid. In chronic forms the rete mucosum is markedly hypertrophied, the papillæ are much enlarged, the vascular changes are pronounced, and cellular infiltration extends deep into the corium.

Diagnosis.—The diagnosis of eczema in infants can usually be made with little difficulty. Scabies, with an accompanying dermatitis, may cause confusion, but the multiform, often pustular, character of the lesions, their tendency to affect certain regions, the presence of burrows, the involvement of the penis in boys, and the presence of scabies in other members of the household, are distinguishing features. Nursing infants may present the eruption of scabies on the face. Various forms of cutaneous syphilis, especially the papular and papulo-squamous type, may bear a resemblance to eczema, especially if they become eczematized, as occurs in some children, and exhibit a tendency to exudation. The bright red, acute, pruritic character of the lesions of eczema are in marked contrast to the dark colored, often circular, infiltrated, non-itching lesions of syphilis, which in addition are apt to occur about the mouth, nose and genitals, and on the palms and soles, and are associated with mucous patches, snuffles, and other evidences of syphilis. Impetiginous eczema may be confused with impetigo contagiosa; the latter is contagious, auto-inoculable, develops as superficial, discrete vesicles or blebs which rupture readily and form yellowish, granular crusts. In newborn infants the lesions of impetigo often are extensive blebs and bullæ. The diagnosis from pediculosis, ringworm of the scalp, and favus is readily made. The differentiation from papular urticaria, lichen planus, and prurigo has been discussed under those subjects. Neurodermitis, which is not uncommon in older children, differs from eczema in its mode of onset and evolution, intensity of itching, continued dryness, and absence of acute phases. It occurs in circumscribed, elevated, infiltrated patches most often in the flexures, on the nape of the neck, upper shoulder region, inner surfaces of the thighs, and on the extensor surfaces of the forearms, or in a diffuse form with a more extensive distribution, and is often complicated with eczema.

Prognosis.—The prognosis of eczema in infants and young children is good as a rule, although in some the disease persists and becomes chronic in spite of skillful and persevering treatment. In patients with a dry, xerotic skin approaching the ichthyotic type, the disease is especially intractable and the prognosis is not favorable for early relief. There is little tendency to spontaneous recovery during infancy, and relapses are apt to occur repeatedly after apparent recovery. When the process is of long duration structural alterations occur in the skin and add to the difficulties of treatment.

Treatment.—The successful treatment of eczema in children depends in most cases on a judicious combination of constitutional and local measures. In some instances the disease yields to local therapy alone, and in others proves rebellious to the most carefully planned measures of both pediatrician and dermatologist.

A careful investigation into the food is essential, with reference to its character, preparation, and quantity, and the frequency and manner of feeding. Errors in diet which can be held accountable for overfeeding, underfeeding, and gastro-intestinal disturbances are to be corrected by appropriate methods. A frequent error is overfeeding, especially toward the end of the first year, through an excess in solid food, usually farinaceous. In infants who are over-nourished the amount of food or the fat of the milk is to be reduced, or a mixed diet must be given. Czerny showed that eggs and the fat of milk often have an unfavorable influence in eczema and advised the substitution of vegetables, fruit, and cereals. When the quantity of milk is decreased, the deficiency may be supplied by cereals as early as the second or third month. Vegetable soups and cereals may be used from the sixth month. After the second year milk may be largely replaced by a vegetable diet with a small amount of meat.

Cutaneous sensitization tests and examination of the stools in many instances provide information which can be utilized to advantage in improving the digestive function and in constructing a proper dietary. Elimination of animal or vegetable proteins which may reasonably be suspected as a result of the cutaneous test, is not always followed by improvement, and this has caused some to discredit the procedure. White, O'Keefe, Engman, and others who have had an extended experience with the sensitization test in eczema in young children are, however, convinced of its value as a therapeutic measure. O'Keefe[45] has pointed out that in addition to eliminating or limiting the intake of offending proteins when possible, it is often necessary to correct a fat or a carbohydrate indigestion in order to secure proper digestion of the protein and thereby relieve or cure the eczema.

Cutaneous sensitization tests are also contributing to clarify the difficult subject of the treatment of eczema in nurslings. O'Keefe's studies show that a large percentage of exclusively breast fed infants are sensitized to foreign proteins (egg, cow's milk, wheat, oat) ingested with breast milk, but not to human milk proteins, and that when the offending protein, to which the mother is herself not sensitized, is omitted or limited in the maternal diet, cure or improvement in more than half of the patients follows. Disappearance of an infantile eczema when chocolate was eliminated from the nursing mother's diet has been observed several times by the writer.

Although at present experience with regard to desensitization in eczema of children is limited, Engman[46] believes that it will prove of considerable value.

Medicinal treatment provides no specific remedy for eczema, but finds its chief indications in the promotion of elimination, relief of constipation, correction of an anemic or atonic condition, and in subduing nervousness. When eczema is associated with asthma, bronchitis and recurrent vomiting, or if the parents give a history of such association, glucose solution, bicarbonate of soda or other alkalies are indicated. Thyroid extract may prove useful in children with dry and harsh skin, or in some cases of seborrhoic eczema. Arsenic is of no value as a rule, though it may prove useful in older children with chronic, infiltrated and scaling forms of eczema. It should never be given in acute attacks. Opium in any form is to be avoided, as it increases the itching. Veronal may be used in small doses as a sedative with good effect. In anemic and strumous children affected with pustular forms of eczema, cod-liver oil and the syrup of the iodid of iron are often beneficial.

The general management of the patient comprises protection against cold, high winds, and strong sunlight. The garments should be light and warm, and the bed-clothes not too heavy, so as to avoid perspiration. Napkins should be promptly changed, used again only after thorough washing and rinsing, and should be sun-dried if possible. The unaffected skin is to be kept scrupulously clean, and the process of washing and drying is to be performed gently and carefully, using a lye-less or other special soap in minimal amount. The skin may then be lightly powdered over with stearate of zinc or a dusting powder composed of magnesium carbonate 4 dr., zinc oxid 4 dr., and boric acid 1 dr. The eczematous surface is never to be washed with soap or plain water, though bran, starch, oatmeal, or borax water may be used when washing is necessary. Most patients must be subjected to some form of restraint to prevent damage from scratching. A good method is to apply splints to the arms on the flexor surface. No device, however, will restrain an infant from rubbing its cheeks against the pillow and thereby inflicting damage.

Local Treatment.—Local treatment is of importance in every case. The underlying principles are to employ soothing remedies in acute stages, astringent applications when the process is subacute, and suitable stimulating remedies in chronic forms of the disease. Soothing ointments and pastes act more effectively when they are applied thickly spread on muslin or lint strips under light bandages. For the face a properly fitted muslin mask is very useful. Stimulating ointments are to be rubbed in with the finger. Before the use of any application it is essential that scales, crusts, and other debris be removed in order that the remedy may come into direct contact with the diseased surface. In most cases the best procedure is to soften crusts on the glabrous skin with olive or almond oil, or white vaselin, and then remove them by washing with a boric acid solution or olive oil. For the removal of crusts on the scalp, and especially if suppuration is present, the boric-starch poultice is invaluable. In all purulent forms of eczema the boric-starch poultice or wet dressings of boric acid are indicated for drainage, followed by a 2 per cent. ointment of ammoniated mercury as a mild antiseptic, though the latter should not be used over large surfaces.

In the acute erythematous and papular stage, sedative and mildly astringent lotions are preferable in most instances. They may be used as wet dressings or are dabbed on the affected parts. Boric acid solution with a small amount of alcohol, followed by talcum, or diluted black wash, zinc and calamine lotion, zinc oxid and lime-water, and the lead and opium wash are all useful. If itching is pronounced 1 per cent of carbolic acid with 2 per cent. of glycerin may be added. White recommends the following lotion: Amyl. maidis, 25.0; talc, 25.0; glycerin, 20.0; aq. saturnin., 100.0; aq. distill., 100.0. If the above preparations are too drying, a bismuth and zinc emulsion, calamine liniment, or an oily cream composed of zinc oxid 8 parts, bismuth subnitrate 4 parts, olive oil 120 parts, and liquor calcis 120 parts (Ormsby) may be used with good effect. In some cases zinc oxid ointment softened with cold cream, or Lassar's paste without salicylic acid, when applied alone or after a liberal application of equal parts of lime-water and almond oil will be beneficial.

In the vesicular and weeping stage, continuous moist compresses of 1 to 2 per cent. boric acid solution with 0.5 to 2 per cent. of resorcin, or the solution of aluminum acetate diluted 1:10, will often cause a rapid subsidence of the acute inflammatory symptoms. It is then proper to employ pastes, such as zinc oxid 1 part, starch 1 part, vaselin 2 parts; or one composed of equal parts of zinc oxid, lanolin and vaselin, applied beneath a light bandage or a mask, until the process has been reduced to a dry stage or resolution is complete. If the eczema resists these measures and continues to weep, ½ or 1 per cent. solution of salicylic acid 2 per cent., and precipitated sulphur 2 per cent., in color. The lesions are often surrounded by a reddish halo and the of silver nitrate may be painted over the parts before the paste is applied. The use of zinc oxid and calamine lotion or similar preparations on moist surfaces is not advisable, as a rule, because they are apt to cake, dam back the exudation, and cause the skin to crack or fissure.

Ointments and pastes often are not tolerated in acute weeping eczema and act as irritants. An exception to this is found in naftalan, first recommended to the writer by Ormsby, which may be used in the most acute types, especially those involving the face, when applied in a paste composed of naftalan 2 parts, zinc oxid 1 part, and starch 1 part, spread on muslin or lint and covered with a mask or bandage. It is renewed twice a day and the parts are cleansed with olive oil at each dressing. The use of crude coal tar in a paste composed of crude coal tar, 2.0 or less; zinc oxid, 2.0; amyl. maidis, 16.0; vaselin, 16.0, is strongly recommended by C. J. White[47] in moist or weeping, non-purulent eczema in any location. The paste is applied in a thick layer without a bandage, and is to be removed completely every 12 hours with gauze and oil of sweet almonds. This paste should be used alone and without the addition of other drugs.

In the subacute stage, with moderate infiltration and thickening, anti-pruritic and slightly stimulating applications are indicated. Salicylic acid, resorcin, and calomel in 1 per cent. strength in zinc oxid ointment are useful. Schamberg recommends a paste containing 2 per cent. each of phenol and calomel. Tar is perhaps the most valuable agent in this stage, but should always be used with caution. An excellent formula for use in the subacute infiltrated, itching eczema commonly observed on the face in children, is that of Hardaway: Zinc oxid 4.0, ungt. picis liquid. 8.0, ungt. aq. ros. 8.0, lanolin 16.0. Subacute, itching, papular forms of eczema as seen on the extremities and trunk often respond favorably to lotions containing phenol and liquor carbonis detergens.

In chronic eczema stimulating remedies are required to secure absorption of the infiltrate. Tar ointment, crude coal tar, and oil of cade are most valuable in this stage, and should be used weak at first and gradually increased in strength later as tolerance is proven. Radiotherapy is valuable in chronic eczema and in the subacute forms with infiltration. Jadassohn[48] recommends the use of *x*-rays in repeated small doses, even in acute and exudative forms of eczema in infants of one to two years old, which prove resistant to other treatment.

Eczema of the scalp is often associated with seborrhea, and after removal of the crusts and scales usually responds well to an ointment of salicylic acid 2 per cent., and precipitated sulphur 2 per cent., in vaselin. In some cases a 2 per cent. resorcin ointment is more effective. In pustular eczema of the scalp, which may be due to pediculosis, a 2 to 4 per cent. ointment of ammoniated mercury is usually of most service. It is often necessary to follow this by a tar ointment to secure complete resolution.

Granuloma Annulare.—Granuloma annulare is a chronic inflammatory disease characterized by papules or nodules which tend to group and form ringed or circular lesions.

Symptoms.—The disorder develops slowly or rapidly, beginning as a deep-seated non-inflammatory infiltration of the skin, and developing into a nodule or ring of nodules, which are firm, elevated, sharply defined, semi-transparent, and white, pink, or rarely purplish in color. The lesions are often surrounded by a reddish halo and the center may be atrophic. The rings vary in size from ½ to 2 in. or more, are round or oval, and through fusion and involution give rise to crescentic and irregular figures. The lesions are usually few in number, or may be numerous, and they show a predilection for the sides and backs of the fingers, back of the hands, and for the wrists, elbows, feet, ankles, neck, and buttocks. The majority of the cases have occurred in children and young adults, the earliest at the age of 16 months.

Etiology.—The cause is unknown. Little[49] has made a careful study of the disease and is inclined to regard it as tuberculous. The prompt response of the lesions to tuberculin in a patient observed by Hudelo, Civatte and Rabut is held by them as evidence of a tuberculous etiology.

Pathology.—The pathologic changes are confined to the corium, and consist of extensive cellular infiltration in the subpapillary regions, with many epithelioid cells and spindle cells of the connective tissue type. Areas of central necrosis occur in the older lesions, and the infiltration is most marked about the coil-glands, hair-follicles, and blood-vessels.

Diagnosis.—Annular hypertrophic lichen planus may resemble granuloma annulare, and is differentiated by its darker color, angular edge, and tendency to be flat-topped rather than rounded.

Prognosis.—The lesions may enlarge and persist for years when untreated. Spontaneous disappearance occasionally occurs, and Little has observed recurrence after two years of freedom. Ulceration of the nodules has not been observed.

Treatment.—Most cases yield to applications of 3 per cent. salicylic acid ointment or plaster, resorcin, ichthyol, carbon-dioxid snow, or radiotherapy, without leaving a trace.

Dermatitis Repens.—Dermatitis repens is a chronic inflammatory disease, usually following an injury, and characterized by a slowly extending serous undermining of the upper layers of the epidermis.

Symptoms.—The disease usually starts after an injury, on a finger or toe with a persistent vesicle or small bleb, or without such early lesion, and thereafter spreads gradually by serous undermining of the epidermis or by the marginal development of new vesicles or blebs, progressing for months and often invading an entire extremity. Within a short time a characteristic clinical picture is produced, consisting of a central area or patch of deep red, raw or glazed denuded rete oozing at various points, and surrounded by a narrow, ragged border of undermined or vesicular epidermis, from beneath which serum and pus can be expressed. The central portion may become cornified and heal while the marginal extension still advances, or it may become eczematous. When healed the epidermis often may be parchment-like, atrophic or cicatrized. Constitutional symptoms are absent, there is no pain and only slight itching.

Etiology.—Crocker believes that the disease is a peripheral neuritis due to injury and that secondary parasitic invasion produces the extension. Sutton has found the staphylococcus aureus in all of the cases seen by him. The disease appears to be an infectious dermatitis.

Pathology.—Sutton[50] found the destructive process confined to the upper layers of the rete, with vesicle or small abscess formation in the granular layer, and separation of the stratum lucidum from the underlying cells.

Diagnosis.—The eruption of infectious eczematoid dermatitis is usually widespread, superficial, and the patches lack the undermined margins and central denuded area of dermatitis repens. In eczematoid ringworm the vesicles are scattered and not marginal, extension by serous undermining of the border does not occur, and the epidermophyton fungus is often found.

Treatment.—The disease is extremely resistant to treatment and may persist for months or years. Sutton advises the use of an autogenous vaccin in large doses, and recommends the daily use of Ruggles mixture (salicylic acid 1 part, tannic acid 5 parts, alcohol 50 parts) painted thoroughly into the margin. Ammoniated mercury ointment, potassium permanganate, formalin, and silver nitrate are also recommended.

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CLASS V. HYPERTROPHIES, ATROPHIES, NEUROSES AND ANOMALIES OF PIGMENTATION

By James Herbert Mitchell, M.D.

(A) Hypertrophies

Clavus.—Synonym.—Corn. This is a circumscribed hyperkeratosis, usually occurring over the phalangeal articulations of the toes, particularly on the little toe, as a result of intermittent pressure due to ill-fitting shoes. It is especially likely to occur on "hammer-toes," and is the cause of much discomfort and occasionally of intense pain.

Clinically, it appears as a hard, somewhat elevated, keratotic mass, in the center of which is a small, semi-translucent cone, which is commonly spoken of as the "root." This mass represents the compressed horn cells, which are imperfectly cornified, and extend into the atrophied derma beneath. A considerable degree of inflammatory reaction is usually present.

When the corn occurs between the toes, usually in the fourth interspace, it becomes macerated and thereby takes on a white appearance as if cooked. This is known as the soft corn.

Treatment.—This consists of (1) removal of the pressure, without which no treatment will be successful, and (2) application of a keratolytic agent such as salicylic acid. This may be applied in the form of salicylic acid plaster, which is left on for several days, after which the center, as a rule, can be lifted out. When this has been accomplished, the pressure is temporarily relieved and the pain ceases. Or the salicylic acid may be applied in combination with cannabis indica in collodion. This mixture is painted on once daily, or more often if necessary, until the clavus is thoroughly softened, and the center or "root" can be lifted out.

Mechanically, the corn can be treated by paring the top or, better, by scooping out the center to prevent the pressure of the shoe being exerted on the center or "root." A better way is to use rough sandpaper or the "corn-file." By the use of either of these the central mass, which is harder than the periphery, is filed away and there results a depression. As a rule, the discomfort is relieved until the depression becomes filled again.

Callus.—Callus, or callositas, appears as a fairly well defined, hard, yellowish or dirty-brown, semi-translucent, cornified plaque. It may occur on any part of the integument as a defensive response to friction or pressure, but usually is found on the palmar and plantar surfaces. It differs from clavus in that there is neither inflammatory reaction nor atrophy in the derma, and there is, therefore, neither pain nor tenderness. Infection occasionally does occur, however, beneath the callus, in which case much pain and a burrowing spread of the infection may result.

The location of the callosities is an indication of the work or play engaged in by the person on whose hands or feet they occur. Thus a violinist will have callosities on the tips of the fingers of the left hand, whereas a guitarist will have similar thicknesses on the tips of the left hand and on the palmar surfaces of the fingers of the right hand as well. Golfers will have horny masses in certain areas, whereas tennis players will have them in other regions. The sweat secretion is, as a rule, unchanged, but there may be a mild hyperidrosis. The tactile sense is reduced in proportion to the thickness of the callus.

Histologically, there is a little change other than a circumscribed hyperkeratosis.

Treatment is unnecessary, inasmuch as there is no pain and the lesions gradually disappear when the causal factor is eliminated.

Keratosis Pilaris.—This disorder, known also as *Folliculitis rubra* (E. Wilson), *Cacotrophia folliculorum* (T. Fox) and *Xeroderma pilaris* (Besnier), is frequently encountered as a follicular keratosis on the outer surfaces of the upper arms and on the outer surfaces of the thighs. Occasionally it may be seen on the back, but it rarely occurs in the cutaneous folds or in the regions where the sebaceous glands are numerous.

The symptoms consist of dryness of the skin, diffuse scaling and acuminate, follicular papules. The appearance of the skin is much like that of xeroderma or of mild ichthyosis. The scaling and dryness, due to insufficient fat, is intensified in winter.

The follicular papule is conical and consists of a keratotic plug, within which is the curled-up lanugo hair. In later years this papule flattens, the hair follicle becomes atrophied and a scar may form. The color of the papule is usually that of the surrounding skin, but in the more marked cases the papule may be red. Brocq distinguishes between keratosis pilaris alba and rubra. The latter is the more severe of the two types and is the more likely to result in scars.

The condition is essentially a congenital malformation of the skin characterized by a deficient number of sebaceous glands and a follicular keratosis. The relation of keratosis pilaris to the nevi and to ichthyosis is a matter for debate. It differs somewhat from the latter in that it may occur in several members of one family, may be delayed in its development until puberty, and normally runs a definite course, clearing partially or completely in adult life.

The **treatment** consists in supplying the skin artificially with oil by external applications. A good application consists of 25 per cent. glycerin in olive oil. This should be applied daily and after each bath. An ointment containing an animal fat base, such as lanolin, in which 1 per cent. salicylic acid has been incorporated, is of value.

Keratosis Follicularis Contagiosa.—Under this title Brooke described a rare disorder characterized by follicular keratoses, of which there were six cases in the children of one family and three cases in the children of another family. The first change is a diffuse keratosis with exaggeration of the cutaneous furrows. Gradually there appear black, punctate, follicular, comedo-like plugs, some of which become horny or spike-like. The lesions commonly occur on the neck, trunk, and flexor surfaces of the extremities. Histologically, two changes are noted in the follicle; simple retention and the formation of horny plugs in the follicles.

The disorder responds readily to external applications of saponified oils, or simple ointments.

Lichen Pilaris Seu Spinulosus (Crocker).—Synonyms.—Keratosis follicularis spinulosa. Lichen spinulosus. Acné cornée.

Symptoms.—This disorder, which was first described by Crocker, is characterized by the presence on various parts of the body of grouped, follicular, pinkish papules, from the center of which emerge short keratotic spines. The spine may be removed, leaving a small cavity in the center of the papule. When palpated the area of grouped papules gives to the hand the sensation of a nutmeg grater. The lesions are usually symmetrically distributed on various parts of the trunk, on the extensor surfaces of the arms, or on the buttocks. The lesions either occur in crops which disappear between exacerbations, or they persist indefinitely. The disorder is most commonly observed in young children, but a few cases have been reported by Graham Little, Beatty, Senear and others associated with folliculitis decalvans of the scalp. Strassberg, who has recently seen a case presenting this combination, is of the opinion that the cicatrizing alopecia of the scalp is an end result of the process in that region rather than a separate disorder.

Etiology.—The cause of the disorder is unknown. Adamson suggests that it may be of toxic origin.

Diagnosis.—Keratosis pilaris differs in that the follicular papules are widely distributed and never grouped, do not occur in crops and the skin is usually dry and scaly.

Treatment.—Salicylic acid, because of its keratolytic properties, combined with oil of cade in a simple ointment base will sometimes bring about a disappearance of the lesions.

Verruca Vulgaris (Wart).—The common wart is a circumscribed, dirty yellow, horny excrescence, which may be slightly or markedly elevated, hemispherical, or pedunculated. The surface may be smooth or mamelonated, and as a rule the lesion on the plantar or palmar surface is surrounded by a cornified collarette. The wart is usually multiple and grouped and may occur in great numbers on the dorsal surfaces of the hands, where it is most commonly seen, or upon the face. It is painless and lacking in tenderness, except when it develops about the nail or upon the plantar surface, where it is constantly exposed to pressure of the shoe in walking.

Warts occur more frequently in childhood and early adolescence than at any other period of life. Especially is this true of the juvenile flat wart known as *verruca plana juvenilis*. This is a flat, hyperkeratotic lesion which does not develop beyond the early flat stage through which verruca vulgaris passes. It differs also from the latter in that in children it is found in greatest numbers on the face, more especially the forehead and temples, whereas verruca vulgaris occurs in greatest number on the dorsal surfaces of the hands. In adult males, however, the bearded region of the face may have hundreds of small lesions of the vulgaris type.

The wart which gives the patient the most discomfort and which offers the greatest amount of therapeutic difficulty is the plantar wart. This type rarely occurs in young children, but is frequently encountered in girls in the early adolescent period. The ball of the foot, the region of the fifth toe, the plantar surface of the great toe and the heel being the points of the foot where the greatest pressure and, therefore, the most trauma occurs are the sites of predilection. When the lesion develops in the thick callus of the ball of the foot, it may be scarcely visible until the surface is pared away with a knife. The trimming discloses a whitish, succulent, circumscribed mass, varying in size from 1 to 10 mm., composed of papillæ in close apposition to one another, and extending deeply downward at right angles to the surface of the skin.

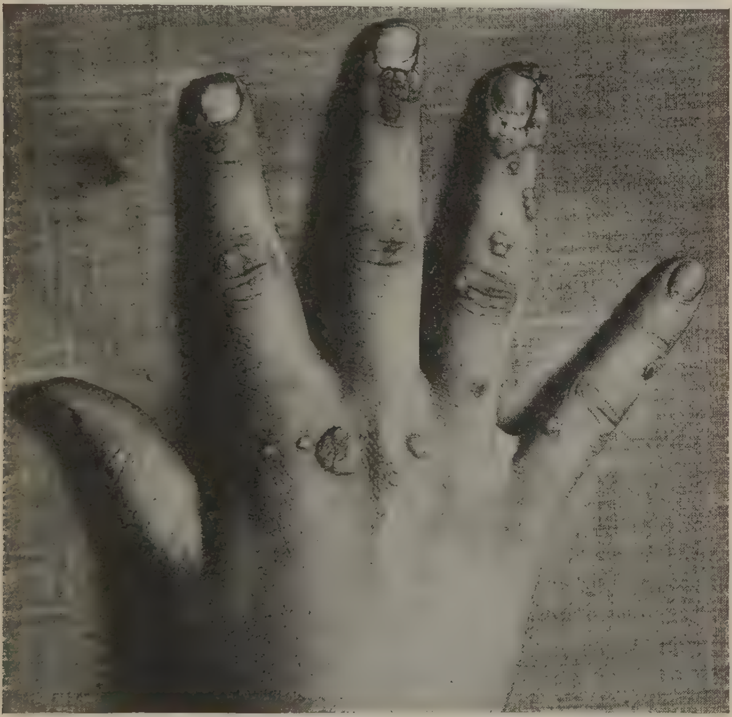

FIG. 54.—Verruca vulgaris, girl. (Fordyce and MacKee.)

Etiology.—The cause of warts has usually been ascribed to one of three factors, namely, trauma, foreign bodies or infection. Trauma, however, is probably only the predisposing factor which creates the portal of entry for one or the other of the two factors mentioned. That the wart is due to infection and that it is contagious as well as autoinoculable seems proved beyond doubt by the wart of Kuhneman, Jadassohn, Variot and recently by Wile. The last named was able to produce the lesions experimentally by epidermic injection of the sterile filtrate from macerated verrucæ.

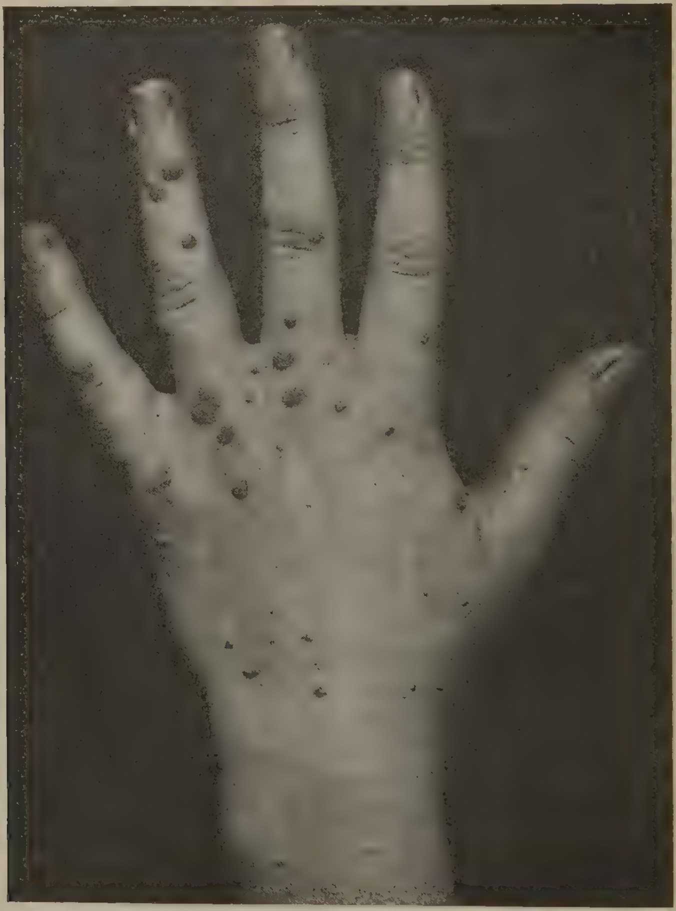

Fig. 55.—Verruca vulgaris, young adult. Appeared also in face and forehead. Some lesions of flat variety as in the young. (Collection of Dr. Grover W. Wende.)

Histologically, the wart begins with an obliteration of the papillæ and a marked hyperkeratosis (verruca plana). Later the vascular papillæ become markedly elongated and there occurs a corresponding elongation of the rete pegs (acanthosis) and hyperkeratosis.

The **treatment** of verrucæ varies somewhat with the location of the lesions. Those on the dorsum of the hand, on the face and in the scalp frequently respond readily to glacial acetic acid. Nitric acid, however, should never be used because of the severe burns and subsequent scarring which may follow its use. Carbon-dioxid snow, when properly used, gives excellent results in all forms of verrucæ,

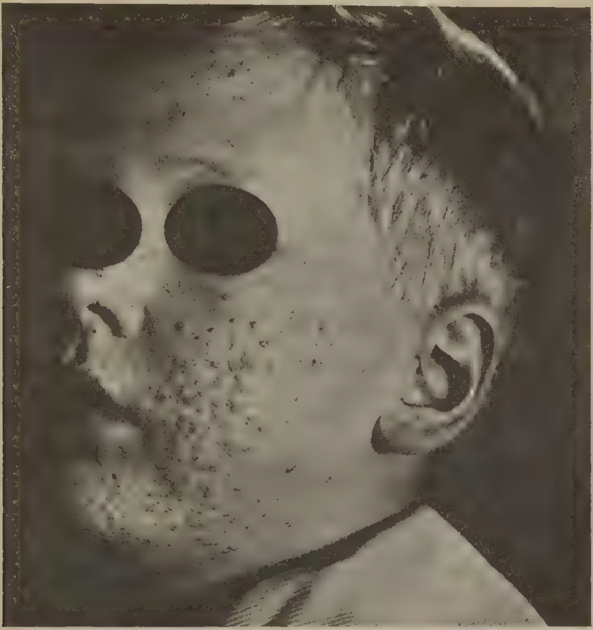

FIG. 56.—Verrucæ planæ. (Fordyce and MacKee.)

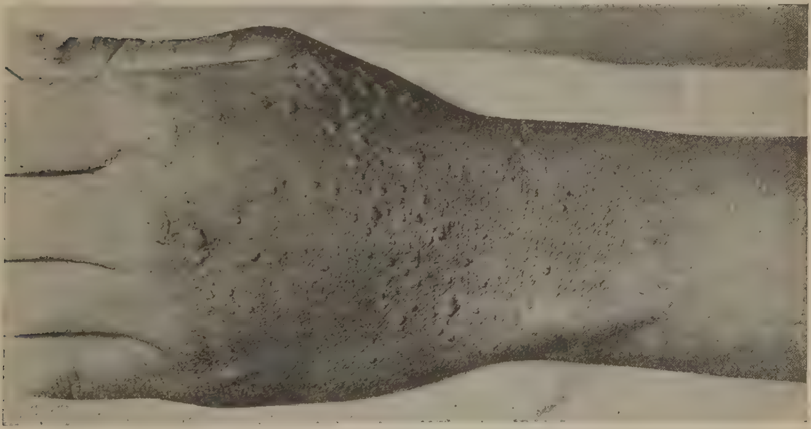

FIG. 57.—Verrucæ planæ juvenilis. (Ormsby and Mitchell.)

but is not applicable in cases of verruca plana juvenilis in which the lesions are very numerous. In these cases liquor calcis sulphuratæ (Vleminckx's solution) applied daily with a swab gives good results.

Chas. J. White has reported complete healing in 10 of 11 cases by the internal administration of protiodid of mercury in ¼ gr. doses.

The plantar wart is best treated by radio-therapy, as also are numerous warts on the hands or face.

Cornu Cutaneum (Multiple Juvenile).—A few rare cases of verrucous nevi occurring in infants and young children, in which the hyperkeratosis was so localized and so marked as to form a horn-like appendage, have been reported by Ingrassias, Fabrice de Hilden, Manssurof and others.

Porokeratosis (Mibelli).—Synonym.—Hyperkeratosis excentrica (Respighi).

Parakeratosis is an extermely rare disorder described independently in 1893 by Mibelli and Respighi. Stelwagon observed a case in 1888 but did not report it.

Symptoms.—The disorder is a keratotic progressive process which begins, as a rule, early and persists throughout life. It is frequently familial, as in the 11 cases in four generations reported by Gilchrist, and in the three generations of the case observed by Wright. The lesion begins as an insignificant, slightly elevated keratosis which enlarges by peripheral extension and simultaneous central atrophy. About the periphery there gradually develops a "dike" in the form of a prism which has an elevation of from 1 to 6 mm. Along the narrow ridge of this "dike," or wall, there is usually to be seen a narrow groove or sulcus having a slight overlapping internal wall. The "dike" is horny and is sharply demarcated from the normal skin. The center of the lesion is usually depressed and atrophic but also somewhat keratotic. The hair-follicles are, as a rule, absent in the center of the lesion. The lesions may vary in size from a few millimeters to an area covering the greater part of the forearm. The areas of predilection are the extremities, especially the dorsa of the hands and feet, the face and the genitalia. In a few cases the lesions have been observed in the buccal mucous membranes. When lesions occur on the face the "dike" is less prominent and the lesions are scarcely more than a mild atrophy.

Etiology.—Nothing is known concerning the cause of the disorder. The early onset, as in the case of Bruck and Hirsch at four weeks of age, the familial tendency, the persistence and the resemblance of the disorder to the nevi have inclined Truffi, Wright and others to class it among the verrucous nevi. Matsumoto's case of extensive linear lesions was probably linear nevi rather than porokeratosis.

Pathology.—The process is apparently initiated by an inflammatory process in the corium which is followed by acanthosis and later by hyperkeratosis of the upper rete and lower corneous layers of the epidermis. The papillary layer of the derma is practically obliterated in the central area.

Treatment.—No method of treatment has proved to be of mucn value. Brocq finds the permanent application of Vigo plaster to give the best results.

Acanthosis Nigricans.—This is a very rare disorder first described by Pollitzer and Janowsky, simultaneously observed and studied by Darier, and later described by the latter under the title of *dystrophie papillaire et pigmentaire.* Darier was the first to establish the connection existing in the adult cases between this dermatosis and abdominal carcinoma. There are two types of the disease, the adult and the juvenile. In the former the patient is usually a female of 30 or more years, having an abdominal carcinoma which in a few cases has had attention directed to it for the first time through discovery of the dermatosis. In this type the case usually progresses to a fatal termination. The juvenile type, however, occurs in children who are otherwise in good health, and gradually undergoes involution, ending in complete recovery. The juvenile type, which is about twice as freqent as the adult type, is, obviously, the only one having a place in these pages.

The fundamental characteristics of the disorder, as described by Darier, consist of (1) a wrinkled condition of the skin with grouped or disseminated papillomatous vegetations and (2) a deep pigmentation. The lesions are regional and symmetrical and occur in the order of frequency in the axillæ, about the neck, the ano-genital region, internal surfaces of the thighs, the face, the cubital and popliteal fossæ, umbilicus, dorsa of the hands, about the nipples and the feet.

The wrinkled condition of the skin is due to an exaggeration of the natural lines of the skin and can readily be smoothed out by traction. It is most marked in the center of the patches and gradually decreases toward the margins. The papillomatous lesions are soft and velvety and are without any indication of hyperkeratosis. In addition to the papillomatous lesions there are usually verrucous lesions which are markedly keratotic.

Etiology.—The cause remains obscure. Nothing is known concerning the pathogenesis, other than that in the adult cases there co-exists abdominal carcinosis.

Diagnosis.—This is simplified by bearing in mind the characteristics enumerated above. *Simple papillomata* do not occur in the same regions and are lacking in the characteristic pigmentation. *Ichthyosis* is congenital and is always scaly, whereas acanthosis nigricans is neither. *Psorospermosis follicularis vegetans* (Darier's disease) differs in having a corneous crust which penetrates the hair-follicle, and in which are enclosed the characteristic corpuscles ("psorospermes").

Treatment is of little avail. The duration of the juvenile form is indeterminate.

Angiokeratoma.—Under this title Mibelli was the first to describe a disorder occurring on the hands and feet of children with pernio or with glandular tuberculosis. Brocq simultaneously described it as "*Telangiectasies verruqueuses.*"

The disease is characterized by the formation of pinhead-sized, bright red, rounded, dilated vessels, the color of which disappears only when much pressure is applied and which reappears promptly after releasing the pressure. The development of one lesion is usually followed by the appearance of satellites which eventually coalesce to form lesions measuring 2 to 3 mm. in diameter. Puncture of a lesion leads to marked hemorrhage. After a time hyperkeratosis of the epidermis covering the telangiectasia occurs and a verrucous lesion results.

The lesions, as a rule, are found on the dorsal surface of the fingers and toes, but in rare cases they have been encountered elsewhere.

Histology.—There is a marked dilation of the papillary and subpapillary vessels, and formation of lacunæ which may extend to the epidermis. Over these cavernous vessels hyperkeratosis takes place.

Etiology.—The etiology is unknown, but the association of the disorder with acro-asphyxia and pernio is a common observation. The lesions appear to develop and undergo involution *pari passu* with the co-existing pernio.

Diagnosis.—The location, the color and the hyperkeratosis make the differentiation between angiokeratoma and the other angiomata, congenital or acquired, quite simple. Lymphangioma has neither the distribution nor the appearance of angiokeratoma. Verruca vulgaris is lacking in the color of angiokeratoma due to the telangiectasia.

Treatment.—The best method of treatment is by means of the electric needle.

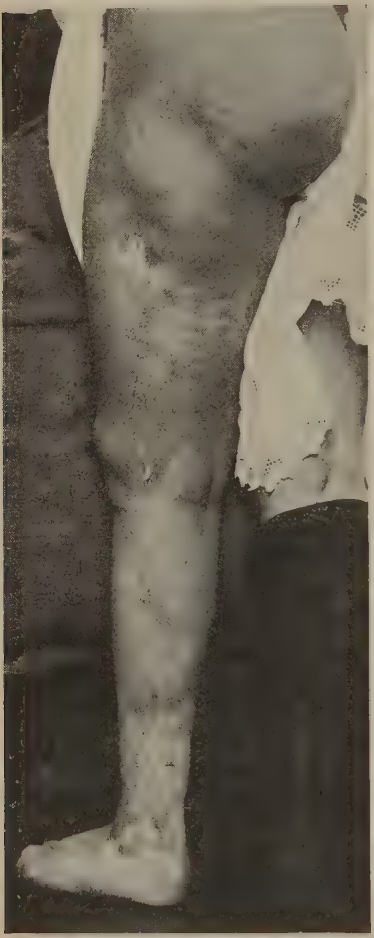

Fig. 58.—Morphea guttata with scleroderma in a girl of 14. Two years duration. Began at ankle and ran upward and inward following course of nerve. Extensive area. (Collection of Dr. Grover W. Wende.)

Scleroderma.—**Synonyms.**—Hide-bound disease. Dermatosclerosis. German: Sklerodermie. French: Sclérodermie.

Definition.—By the term scleroderma is understood a group of cutaneous disorders more or less related and characterized by a diffuse or circumscribed, indurated, thickened condition of the skin and subcutaneous tissue, and which terminates in atrophy and pigmentation.

Symptoms.—Diffuse scleroderma may have a sudden onset without prodromal symptoms, or it may develop gradually with a sensation of restriction in movements of the parts involved, and accompanied by neuralgic pains. An infiltration or edematous process which is hard and deep-seated makes it impossible to pick up the skin between the thumb and finger. The edema is peculiar in that it imparts to the finger a sensation of lard. The color may be unchanged or the skin may take on a dirty-yellow or become pigmented. The upper extremities are most commonly affected, with the trunk and the head and neck next in order of frequency. When the joints are involved they may become immobile. The face becomes expressionless and takes on a mask-like appearance. Movements of the lips and jaws may become so impeded as seriously to interfere with the taking of nourishment. The skin of the thorax may be transformed into an inelastic cuirass which prevents deep inspirations. The duration of the edematous or stage of infiltration is variable. The edematous stage gradually gives way to a process of sclerosis and later to atrophy. The subcutaneous fat completely disappears and the skin becomes fixed to the underlying structures. In some cases even the musculature of the involved regions may undergo atrophy. Ulceration may occur over bony prominences. The color gradually becomes more pronounced and pigmentation increases. In some cases areas of de-pigmentation co-exist with hyper-pigmentation. The sensitiveness of the skin is usually unchanged, but a sensation of cold or paresthesia may be present.

Scleroderma in children is usually more acute and the resulting atrophy less severe than in adults. In some cases the progress of the disorder may become arrested and, as in the case reported by Goodman, clear up without sequelæ.

In infants the process may be of very early onset after birth and of short duration. Lieberthal reports a characteristic case in which there developed on the ninth day a bluish-red, slightly elevated and indurated discoloration on the upper part of the back. Two days later a similar spot appeared on the left shoulder. Eventually the lesions coalesced until they covered the greater portion of the back. There was no pitting on pressure. The process cleared up completely within six weeks after onset without leaving a trace of the disorder.

The course of scleroderma varies to a marked degree. The disease is essentially chronic and lasts for months or years. The patients are likely to succumb to pulmonary infections or to nephritis.

Circumscribed Scleroderma (Morphea, Keloid of Addison).—Morphea begins by the development of a small violet or pink macule. This macule gradually enlarges until it attains the size of a lentil or even that of the palm. The center becomes blanched until it takes on the tint of old wax or old ivory, and meanwhile a lardaceous induration occurs. The center is usually level with the surface of the skin (*alba plana* type), but may be elevated or mammillated (*tuberosa* type). The surface may be smooth and shiny or covered with fine squames. In some cases telangiectasia may be present. About the periphery is a lilac halo (*lilac ring*) which gradually shades off into the ivory hue of the central portion. There is little or no subjective sensation, but formication may be present. The hairs of the region involved fall, the secretions cease, and the tactile sensation may be greatly decreased.

After a variable length of time involution of the lesion takes place. In rare cases ulceration may occur. As a rule vascularization is gradually set up, the epidermis becomes scaly, suppleness of the area returns, and eventually little or no trace of the lesion remains.

Instead of occurring in round or oval patches, the lesions may be in bands and extend the entire length of an extremity. The two forms may co-exist in the same patient.

Morphea Guttata (White Spot Disease).—In this variety the lesions vary in size from 1 to 5 mm. and are found usually on the upper chest, shoulders and arms. The lesions may coalesce to form patches with pigmented margins. Atrophy gradually supervenes and a thin, white, parchment-like epidermis is left.

Etiology.—The cause of scleroderma is unknown. It occurs about three times more frequently in females than in males. The diffuse form is encountered most frequently between the twentieth and fortieth years, but may occur at any age. Levin has recently reported a case with extensive lesions in a boy 10 years of age. The circumscribed form occurs at all ages and is frequently seen in infancy. Various physiologic or pathologic processes such as exposure to cold, pregnancy, suppression of menstruation, emotional disturbances and infectious disease, especially syphilis, have been ascribed as causes both by the patients themselves and by attending physicians. The relation of the disease to a disturbance of the endocrines, particularly of the thyroid, has long been observed. The disease is more often seen in association with hypothyroidism than with hyperthyroidism. Schamberg has seen morphea occur in a child of four years in association with typical cretinism. Co-existence of diffuse scleroderma and Raynaud's disease has been noted by Balzar and Golliot. Traumatism as a cause has been cited in forty cases collected from the literature by Thibierge, but after a study of the case reports Thibierge concludes that traumatism is merely a contributory factor, or coincidental. Chronic arsenic poisoning has been demonstrated in three consecutive cases of diffuse scleroderma at the Massachusetts General Hospital by Ayres.

Treatment.—In the management of either the diffuse or circumscribed forms of scleroderma both systemic and local treatment should be instituted. The condition of the general health of the patient should be carefully investigated and symptomatic and tonic treatment begun at once. In some cases a change of climate is of value. If endocrine disturbances are demonstrable the necessary organotherapy is indicated. When hypothyroidism is present the administration of thyroid is usually attended with excellent results. When syphilis co-exists anti-syphilitic treatment may have no appreciable effect on the lesions, as in the case reported by LeChaquet.

Locally, massage, electricity and baths of various kinds, particularly sulphur baths, have been found useful. Brocq advocated the use of electrolysis in the circumscribed forms. The needle should penetrate all parts of the plaque every eighth day with a current of one to three milliamperes for a period of 20 seconds. The needle should be introduced parallel with the surface of the skin in order not to come in contact with the normal skin.

Dermatolysis (Cutis Laxa; Cutis Pendula).—This term has been applied by Bazin to an unusual elasticity of the skin of certain regions associated with hypertrophy of all the largest glands of the skin. According to Alibert there is a palpebral, facial, cervical, ventral and genital form. The elasticity may be so great that the skin of the chest may be drawn over the face. Owing to a hypertrophy of the glands, follicles and subcutaneous connective tissue, the skin hangs in large folds. The skin is soft and pliable and there is usually a variable amount of pigmentation and tumor formation closely resembling that of fibroma molluscum. Some authors are of the opinion that the condition is closely akin to that disorder. Dermatolysis is usually congenital but may be acquired.

Brocq finds that three affections of dissimilar nature have been grouped under the term dermatolysis: (1) Deformity characterized by an exaggeration of the suppleness and the distensibility of the skin (*cutis hyperelasticum*) and which is congenital and hereditary; (2 deformities resulting from the abnormal distension of the integument during pregnancy, obesity, ascites and senility; (3) veritable tumors analogous to the large tumors of fibroma molluscum and which should be considered as belonging under that category.

(B) Atrophies and Neuroses

Ainhum.—Under this title Silva Lima first described a tropical disorder affecting adult members of various colored races, characterized by the formation on the plantar surface of the toe, usually the fifth, of an annular constriction which slowly progresses until it has completely detached the toe. Castellani states that the disease is more common in females than males, in adults than in children, and though it can be found at any age is most common between 30 and 35 years.

The onset is insidious, but may be preceded by trauma. On the plantar surface of the toe a semi-circular fibrous constriction begins and slowly extends until it has encircled the toe, which becomes soft, swollen and discolored. Eventually the toe may be attached only by a pedicle upon which it may be turned about.

Diagnosis.—Ainhum attacks only the toes, differing in this respect from *congenital amputation*, which may occur at any level of an extremity. *Scleroderma annularis* usually occurs on the leg, the fingers, or on the forearm, and undergoes involution without amputation. *Lepra mutilans* is associated with disturbances of sensation, atrophy of the thenar and hypothenar muscles, and other symptoms of leprosy.

Treatment.—Section of the fibrous tissue is sometimes of value early in the disease. Later on amputation must be resorted to.

Pruritus.—Primary pruritus is a sensory disturbance of the skin characterized by intense itching, burning or pricking sensations, unaccompanied by any visible or demonstrable structural change except those which occur secondarily from the scratching. The itching varies in degree in different individuals and at different times of day. It is usually worse late in the day and at night, and the attacks may recur during certain hours each night. The character of the itching likewise varies in different individuals. In some cases it is described as a sensation of ants crawling over the skin (*formication*), in others as a pricking and burning. As a rule, however, it is an almost intolerable itching which comes on in paroxysms and the desire to scratch is irresistible. It is much more frequent in persons of middle life or advanced years (*pruritus senilis*) but does occur in children.

The paroxysms may be so severe that the patient scratches and tears the skin until blood is drawn. In some cases the pain and discomfort set up by the trauma acts as a counterirritant causing the patient to forget temporarily the itching, or else actually assuages the itching for the time being.

The itching may be generalized (*pruritus uiversalis*) or localized (*pruritus localis*). When localized it commonly occurs about the anal region (*pruritus ani*) or about the external genitalia (*pruritus scroti* or *vulvæ*). Both the anal and genital forms are common in adults but very rare in children. When either form occurs in a child it is usually due to intestinal worms.

Pruritus narium results from irritation of the Schneiderian membrane and occurs in people coming in contact with proteins to which they are sensitized. It is most commonly seen in hay fever.

Pruritus hiemalis (winter itch) is frequently encountered in northern climates and results from the wearing of woolen underclothes and drying of the skin due to steam-heated rooms, cold weather and excessive bathing. The disorder usually comes on with the first cold weather and disappears with the coming of spring. In this condition the skin is dry, moderately scaly and there is usually a variable degree of xerosis or keratosis pilaris.

Bath pruritus occurs occasionally in an individual in whom pruritus immediately follows a bath and lasts for several hours. Neither the temperature nor the character of the water nor the nature of the soap seems to be a factor. This type of pruritus is, as a rule, congenital and lasts throughout life.

Etiology.—The causes of pruritus are many and varied. Most of the general or predisposing causes which operate in adults are not to be found in childhood, and therefore need not be mentioned. In children gastro-intestinal intoxication, either because of ingestion of certain articles of diet, particularly proteins, or because of improper elimination, will be sometimes found to be the etiologic factor. Other intoxications such as occur in diabetes, icterus, nephritis, and ingestion of such drugs as opium, morphine, caffein, belladonna, arsenic, and cocain may cause severe pruritus. Occasionally after a prolonged attack of urticaria, scabies or pediculosis, the itching will persist for some time after the pruritic dermatosis has ceased to exist.

Diagnosis.—The diagnosis is made without difficulty, inasmuch as the excoriations are proof of the itching. Every effort should be directed toward removing the cause if one can be discovered. One should always be on guard against overlooking the presence of scabies or pediculi, because in the former the number of galleries will be in inverse ratio to the cleanliness of the patient, and the latter may escape observation unless one makes a careful examination. Moreover, the traumatic dermatitis resulting from a long-standing primary pruritus and scabies may closely resemble each other.

Treatment.—The general condition of the patient should be carefully investigated and any of the above mentioned causes of pruritus, when found, should be eliminated if possible. Opiates should not be administered except in the most intractable case because the narcotics, especially opium and its alkaloids, eventually aggravate rather than alleviate the pruritus. Acetyl salicylic acid almost always and quinin occasionally will give much relief.

Externally, care must be exercised that no wool comes in contact with the body. Bathing should, as a rule, be restricted to the minimum. Hot water abates the itching temporarily but later intensifies it. Phenol in ointment or lotion is an excellent anti-pruritic but must be used with caution because of the toxic effects of absorption when used over large areas, and because of the necrosis which may follow when the phenol settles to the bottom of the container. Menthol combined with salicylic acid and corn starch in petrolatum is of value. The following formula will give good results in some cases:

℞	Liquor carbonis detergens	15
	Lotio nigræ	
	Olei olivæ āā ad	240

Sig.—Apply externally.

Trichotillomania.—Hallopeau was the first to describe and give a name to this condition. It consists essentially in an impulse, which amounts to a mania, to pull out the hairs in certain regions of the scalp. It may be induced originally by itching or other sensations in the regions, but may continue as a habit spasm or *tic d'épilation* long after the pruritus has ceased.

The condition is not to be confounded with the wearing away of hairs of certain regions due to friction or scratching, such as occurs in eczema or other rebellious itching dermatoses.

The disorder may occur even at two years of age, as in the case reported by Graham Little. In this case there was an area of alopecia over the right parietal eminence in which the follicles were intact but from which the hairs had been epilated. The child could be observed to epilate the hairs at all hours of the day but not in her sleep. There was no other neuropathic symptom.

Treatment.—This is a problem for the neurologist rather than the dermatologist to solve. Clipping the hair closely is of considerable value in breaking the habit. An effort should be made to eradicate any localized pruritus that may be present.

(C) Pigmentary Disorders

Lentigo.—Synonym.—Freckles. Freckles are small, circumscribed areas of pigmentation, varying in color from a light yellow to a deep brown. They occur chiefly on the face and hands of blondes, especially of blondes with red hair and fair skin, but they also occur on the unexposed areas. They may be, in rare cases, congenital, but, as a rule, develop between the ages of 8 and 14. Once developed they may persist throughout life. Exposure to the rays of the sun usually intensifies them, and after cessation of exposure they undergo partial involution.

Etiology.—Freckles closely resemble the pigmented nevi and probably are to be included with them. In some cases the lesions may be elevated as are nevi. Pigmentations similar in appearance may occur in senile skin as a result of exposure to the elements (ephelid).

Histology.—The only change is a deep pigmentation of the lower cells of the prickle-cell layer.

Treatment.—Any treatment is futile. Protection from the rays of the sun will prevent the intensification.

Chloasma.—The term chloasma is rather loosely applied to various forms of circumscribed areas of pigmentation occurring on various parts of the body. It differs from lentigo in the marked irregularity of the contour and in the size of the lesions. The color may vary from yellow to deep brown, and different areas in the same individual may vary in the amount of pigmentation, according to the regions involved.

Kaposi distinguished four forms of chloasma: (1) Traumatic, due to friction, excoriation and pressure; (2) caloric, due to heat and light; (3) toxic, due to irritants, and (4) symptomatic, of which there are two subdivisions: (*a*) Uterine and (*b*) cachectic.

The first three, however, representing nothing more than pigmentation which results from chronic irritation, are better grouped as *chloasma idiopathicum.*

The uterine form of chloasma *symptomaticum* has no place in this discussion. The cachectic form includes those pigmentations which occur in severe systemic disturbances such as tuberculosis, syphilis, Addison's disease and Graves' disease. Long continued gestation of arsenic leads to marked, diffuse pigmentation which may persist for years.

Diagnosis.—The failure of the pigmentation to disappear under pressure differentiates chloasma from hyperemia. In tinea versicolor scaling and the fungus (microsporon furfur) are present.

Treatment.—Treatment should include the removal of the cause, if possible. Locally, the application of a 1 per cent. alcoholic solution of bichlorid of mercury is used in some adult cases, but the application of this strong preparation would rarely be advisable in children.

Vitiligo.—This is an acquired cutaneous dyschromia characterized by the development of depigmented, round or oval macules, surrounded by areas of hyperpigmentation. The lesions may be few or numerous, and large or small. They begin as very small macules and very slowly enlarge peripherally until, by coalescence with other areas, the entire cutaneous surface may become involved, or a few lesions may appear and remain unchanged for years. There is no change of any kind in the skin of the areas involved other than the loss of pigment, nor is there any change in tactile or pain sense. The lesions are usually symmetrically distributed and have a predilection for certain areas such as the dorsal surfaces of the hands, the forearms, the neck and the external genitalia. In the summer, owing to hyperpigmentation of the normal skin as a result of exposure to the sun, the depigmented areas become more conspicuous than in the winter. The hair within the area is usually depigmented as well as the skin.

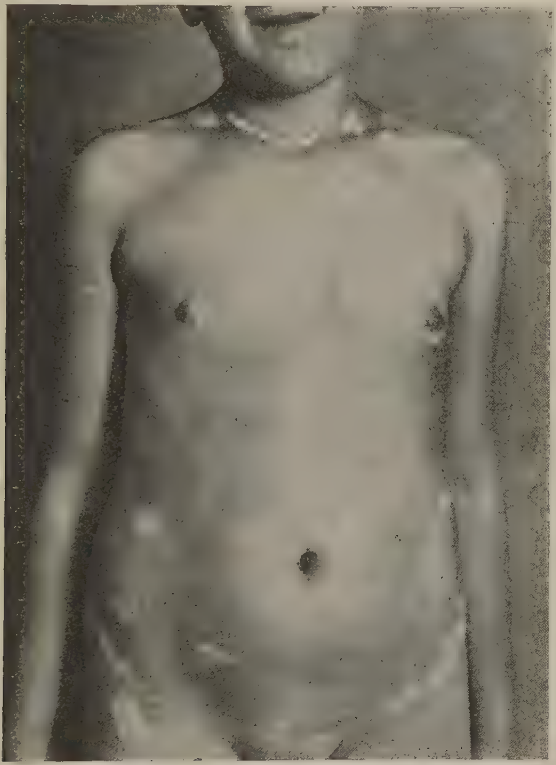

FIG. 59.—Vitiligo, girl. (Fordyce and MacKee.)

The etiology of vitiligo is unknown. The negro appears to be more frequently affected than the whites. The disorder rarely develops before the age of 10 but it may occur in infancy. Shock has long been supposed to be an etiologic factor but the history of shock can only rarely be elicited and even then it is probably only a coincidence.

Pathology.—In the white areas no pigment is to be found in the basal cells but the pigment is abundant in the basal cells of the hyperpigmented area surrounding the areas, and also in the derma where it is contained in round cells in the papillary body, especially about the blood-vessels, follicles and the glands.

Diagnosis.—The diagnosis as a rule is not difficult. Chloasma is to be distinguished from the hyperpigmented areas of vitiligo by the convexity of the margins of the pigmented area. *Pityriasis versicolor* likewise has convex borders, is scaly and in the scales microsporon furfur can readily be demonstrated. *Leucoderma* lacks the hyperpigmented border and in the acquired type changes other than simple achromia are to be seen. *Morphea* has a lardaceous infiltration, is yellowish rather than milk white, lacks the hyperpigmented zone and is surrounded by a lilac ring. In *leprosy* hyperpigmented and depigmented areas may occur which closely simulate vitiligo, but the history, the anesthesia, and other concomitant symptoms will establish the diagnosis.

Treatment.—Various methods of treatment have been used but with little or no success.

Leucoderma.—This term is used by some authors to denote a condition characterized by a congenital absence of cutaneous pigment in localized areas. By others the term is applied to acquired areas of loss of pigment due to local changes such as those resulting from syphilis. The congenital type is most commonly observed in the negro, and occurs as rounded, oval or linear areas of depigmentation. The areas may be located on any part of the body but are frequently seen on the trunk along the course of a nerve. It may be said to be the opposite of a pigmented nevus. The congenital form differs from the acquired form in that in the former the achromia is the only change, whereas in the latter there are usually other changes such as scarring or atrophy.

Diagnosis.—The congenital form or *nevus achromicus* is to be differentiated from *nevus anemicus* (Vörner) by the reaction of the latter to friction. If the nevus anemicus be rubbed vigorously with ice the surrounding skin will become markedly hyperemic, whereas the center will remain unchanged because there is a congenital deficiency of blood-vessels in the nevus area.

Treatment.—Treatment is useless in both the congenital and acquired forms.

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CLASS VI. ACQUIRED NEW GROWTHS OF THE SKIN

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Cicatrix.—Definition.—A cicatrix or scar is a connective tissue new formation, which replaces a loss of tissue either by disease or trauma.

Symptomatology.—The shape, size and texture of a scar occurring in a child depends on the extent and depth of the original tissue loss, that is, it may be linear, circular, irregular, smooth or rough, soft or firm. Recent scars are darker in color and gradually fade to white in the course of years. Cicatrices can be classified as *atrophic* and *hypertrophic*. Of the former the most common varieties originating in childhood are those due to small-pox, chicken-pox, congenital syphilis, acne, the tuberculids, and in rare cases dermatitis gangrenosa infantum or hydroa vaciniforme. Radiating scars about the mouth or atrophic scars on the buttocks are suggestive of congenital syphilis. The hypertrophic scars are chiefly of a traumatic nature, after infected wounds or after extensive destruction of the derma by a burn. The scar following lupus vulgaris or scrofuloderma is often dense and thick. A distinguishing feature of a cicatrix is that it does not extend beyond the limits of the original damage to the skin and may, by contraction, be considerably smaller. Subjective symptoms are inconspicuous, a variable amount of burning or pain being due to pressure on nerve fibers.

Etiology.—It is obvious that a scar may be either traumatic or pathologic in origin. Loss of the epidermis is not followed by scarring unless the corium is also involved.

Pathology.—A fully developed scar consists of interlacing bundles of coarse connective tissue fibers with absence of normal cutaneous structures, such as hair, glands, etc. In the early stage of granulation tissue newly formed blood-vessels are a conspicuous feature, but later become obliterated. The occurrence of sarcomatous and epitheliomatous change in scar tissue has been emphasized by Bloodgood and Heidingsfeld.

Treatment.—Scars are permanent and in the great majority of cases no treatment is indicated. A wide irregular scar may be improved by excision, substituting a linear scar. Plastic precedures or skin grafting rarely improve the condition. Sibley mentions a number of measures which have been efficacious in the treatment of the scarring resulting from acne and small-pox. Among these are Bier's suction cups, radiant heat, hot air and massage combined with such desquamating and exfoliating agents as salicylic acid and resorcin. The repeated hyperemia which is produced causes an increase in vascularity and improves the nutrition of the skin. Of the various electrical procedures, such as ionization, *x*-ray, high-frequency currents, galvanization, and radium, Sibley prefers ionization as by this means a drug soluble in water can be driven directly into the scar tissue by means of the constant current. Sodium chlorid is most useful as a solvent of scar tissue, although iodin and sodium salicylate have also been used. The author has had good results in the treatment of hypertrophic scars with both *x*-ray and radium. The scars become smoother, flatter and more pliable. Fibrolysin (15 per cent. solution of combined thiosinamin and sodium salicylate) is used in 15 minim doses, injected intramuscularly or around the affected tissue every two or three days, but the results have not come up to expectations. When contractures are present multiple deep incisions with a tenotome have been advised, followed by rubbing thiosinamin solution into the wound plus mechanical stretching. Galvanism may be useful in restoring the tone of muscles adjacent to the scar tissue.

Keloid.—Definition.—A keloid is a fibrous newgrowth in the corium, resembling a hypertrophic scar.

Symptomatology.—A keloid arises often at an early age as a firmly imbedded nodule in the skin, either at the site of a previous trauma or in scar tissue. The nodule grows slowly, spreads out laterally over the surrounding skin, and at times reaches a large size, even from 6 to 10 in. in diameter. There may be one or many tumors. In one of the author's cases there were 25 keloids on the face, neck and chest. The sites of predilection are the sternum, probably owing to the frequency of trauma or irritation at this site, the face, neck and trunk. The outline is irregular, band-like or plate-like, with lateral claw-like projections. The surface is smooth, irregularly rounded or lobulated and presents a shining pink or red color. The majority of the tumors are elevated about ¼ to ½ in. above the surrounding skin. Pedunculation is common in the negro race. The author has recently observed a young colored girl with an immense lobulated keloid the size of a fist depending from each ear. This began at the age of nine, following the piercing of the ears. Subjective symptoms, as itching or burning, are often complained of. Keloids in the young have a greater tendency to spontaneous involution than those in older persons.

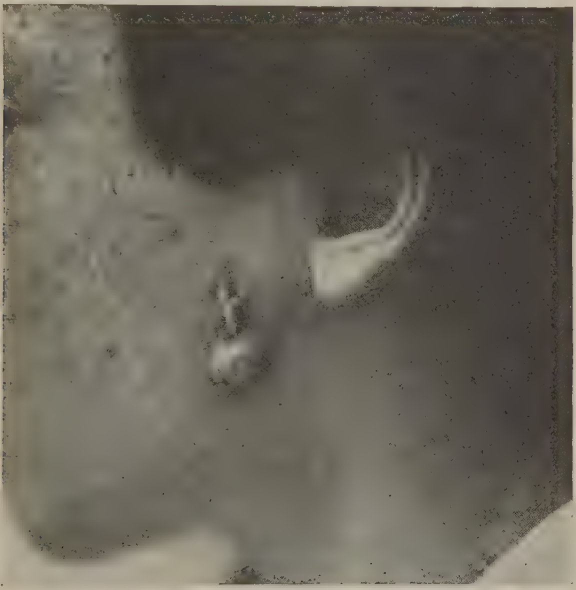

FIG. 60.—Keloid in a girl 8 years of age.

Etiology.—At the present time it is definitely established that a keloid always arises as a result of an injury or at the site of a scar (cicatricial keloid). The existence of a spontaneous, so-called, idiopathic keloid is denied because of the impossibility of excluding traumatism, as a factor in early life. A congenital case has been reported by Bryant. Fagge suggests an intra-uterine skin lesion. Heredity plays a rôle occasionally (Hutchinson) and several cases in the members of one family have been observed by Hebra and Erasmus Wilson. Older infants are occasionally affected as well as children of various ages, although the growths are commoner in adults. Keloids have been known to originate in childhood following burns, cuts, abrasions, bites, ear-ring punctures, as well as in the scars of syphilitic and tubercular lesions, acne, furunculosis, chicken-pox, small-pox and after minor operations. In all probability there is a special individual predisposition toward the development of keloids although the exact cause is not known. The negro race is especially predisposed and cases are seen much more frequently in the colored race than in the white. Tuberculosis is claimed by French dermatologists as a predisposing factor. Justus claims a causal relationship between hyperthyroidism and keloid formation.

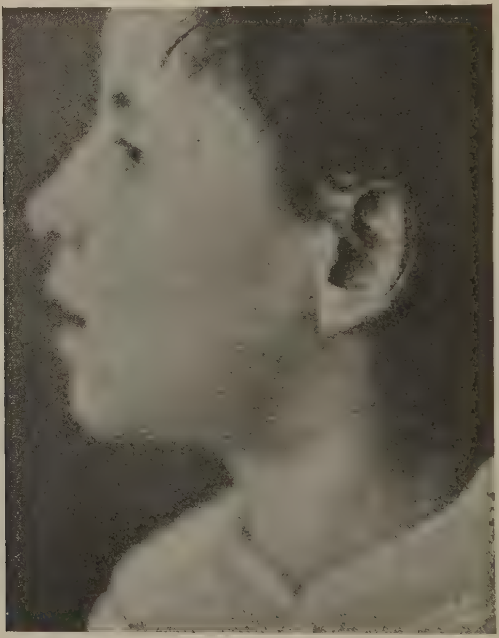

FIG. 61.—Keloid after treatment with radium.

The so-called acne keloid or dermatitis papillaris capillitii is a combined keloidal and sycosiform eruption at the mouths of the hair follicles on the back of the neck and occurs only in the adult male.

Pathology.—A keloid is composed of broad fibrous connective tissue bundles in the corium running parallel to the surface and separated from the thinned epidermis by an area of loose connective tissue. Small, densely staining nuclei are observed between the fibrous bundles. Glands, muscles and hair follicles are pushed aside by the growth.

Diagnosis.—The features of a keloid, especially the color and consistency, are so characteristic as to permit a ready differentiation from other cutaneous tumors.

Prognosis.—Keloids usually become stationary after attaining a certain size. Ulceration and malignancy are rare. Recurrence is the rule after surgical interference.

Treatment.—The various methods of treatment that have been employed from time to time may be summarized as follows: (1) Roentgen therapy is today considered the method of choice and results in a rapid shrinkage of the tumors. The Roentgen-ray may be employed either in broken doses or as filtered massive doses. MacKee, Pfahler and other roentgenologists have reported gratifying results with the modern Coolidge technique, especially in recent small rapidly growing keloids. Pfahler advocates early diagnosis and irradiation of keloids. Care must be used in dosage to avoid sequelæ. Involution is usually rapid with fractional doses and an erythema is to be avoided.

2. Radium is given the preference over *x*-ray in the treatment of keloids by Abbe, Simpson and others, but Knox and MacKee have not found any difference in the efficacy of the two agents. Radium tubes are perhaps more useful in the linear keloid and in circumscribed growths plaques can be conveniently used.

3. In pedunculated keloids excision is permissible if preceded and followed by roentgen therapy (Pfahler). Ordinarily surgical procedures are to be condemned because of rapid recurrence.

4. Freezing with carbon-dioxid snow combined with radium has been successfully used by the author, but must be used with care.

5. Electrolysis and linear scarification are no longer to be recommended.

6. Injections of thiosinamin in 10 to 15 per cent. solution in equal parts of glycerin and water, as originally recommended by Tousey, may be tried but recent reports are not as favorable as earlier ones.

7. Various internal remedies, as arsenic and thyroid extract, are probably without value.

8. External remedies to relieve pain include ichthyol, iodin, mercurial or lead plaster, but these have very slight usefulness.

9. Unna and other German authors have recently utilized the digestive properties of pepsin and hydrochloric acid in the removal of keloids and cicatrices. They advise compresses of a solution containing pepsin 10 c.c., muriatic acid 1 c.c., phenol 1 c.c. and distilled water to make 200 c.c.

Lipoma.—Definition.—Lipoma is a fatty tumor which occurs in diffuse or circumscribed forms and occasionally develops in childhood.

Symptomatology.—The occurrence of congenital lipomas has been pointed out by Jacobi, and more recently by Ransohoff, who reported two cases in which the tumor was located in the cheek. Most congenital lipomas are diffuse and non-encapsulated, their shape irregular and not spheroid as in the adult. They may develop in any part of the body but occur particularly often on the back, occiput, the lumbar and gluteal regions, the abdomen and the calves of the legs. They may be found on the hands and feet in connection with congenital hypertrophy of these parts. Other juvenile cases have been described in the tongue, cervical region, groin and eyelids. Associated congenital malformations as spina bifida, encephalocele, dermoids, or vascular nevi are often present. In certain disturbances of the internal secretions there is a general hypertrophy of fat, as in the well-known Fröhlich's syndrome, or dystrophiaadi poso-genitalis, associated with tumors of the hypophysis. In cretins lipomas may be found at the root of the neck. Lipomas often occur in the skin concurrently with the general adiposity of acromegaly and gigantism. A symmetrical nodular lipomatosis of hereditary type has been described with tumors developing at the time of adolescence. Dercum's disease or adiposis dolorosa, presenting as its cardinal symptoms lipomatous tumors, pain, asthenia, and psychic manifestations, is a disease of adolescent females, but has developed exceptionally as as early as the eleventh or twelfth years. Lyons mentions the case of a woman with Dercum's syndrome whose daughter developed two lipomas in early childhood.

The growth of lipomas in childhood is somewhat faster than in the adult cases. Kirmisson mentions a lipoma which at the end of the first year of life had grown to a size of 20 in. Clinically, lipomas are characterized by their soft, lobular consistency and free movability.

Etiology and Pathology.—With the exception of the rare congenital cases most lipomas are acquired. Little is known of the etiologic factors. In certain cases a disturbance of the internal secretions is a possible factor in the process. Anatomically, lipomas consists of lobulated masses of fat-globules held together by connective tissue.

Prognosis and Treatment.—Lipoma is the most benign of all new growths. The treatment for lipomas is excision.

Telangiectasis.—Definition.—A telangiectasis is a dilatation of a pre-existing cutaneous capillary, with at times the formation of new vessels.

Symptomatology.—It is often difficult to decide in the case of infants or older children whether the telangiectasis is acquired or congenital. In the latter instance it would belong to the capillary angiomata. One of the commonest types occurring in children is the "spider nevus" or nevus araneus, which presents as a central punctiform red dot with radiating lines diverging from it. It occurs as one or more lesions on the face, more rarely on the neck and trunk, often following a slight trauma, and may undergo involution. In other cases telangiectasis are more generalized, presenting as arborizing lines, networks or circles, or forming slightly elevated projections resembling purpura. Crocker pictures a child of seven years with enormous numbers of dilated vessels which continued to appear up to the age of 14.

Telangiectasia occurs as a concomitant feature of various dermatoses in childhood. Thus it is found in adenoma sebaceum, in xeroderma pigmentosum, occassionally in lupus vulgaris, and after *x*-ray or radium dermatitis. In the condition known as Majocchi's disease, occasionally found in children, minute telangiectatic lesions develop on the lower extremities and spread peripherally forming rings, succeeded by purpuric and atrophic lesions.

Telangiectases also occur in childhood as symptoms of a general circulatory disturbance. Children with delicate skin, poor circulation, cyanotic hands and feet, subject to pernio are liable to develop telangiectases on the cheeks. In certain rare cases following one or more attacks of chilblains minute vascular dilatations appear on the dorsal aspects of the fingers and toes which are subsequently followed by warty thickenings of the epidermis. This constitutes the disease known as angiokeratoma or "telangiectatic warts," of which several cases may appear in one family. Telangiectasis has also been described in connection with exophthalmic goiter, syphilis (Stokes), and later in life with hepatic disease. Fearnsides has described five cases of telangiectasis in children in connection with wasting and protracted diarrhea. The lesions were mostly on the limbs and associated with them was an erythema and in two cases a purpura.

An interesting group of cases occurring in a familial type with recurring epistaxis and other hemorrhages associated with multiple telangiectasis of the skin and mucous membranes has been described by Osler, Parkes-Weber, Chauffard and about a dozen authors since then. Hanes has called this condition "hereditary hemorrhagic telangiectasia." The chief symptoms are the localized groups of telangiectases on the skin of the face, and on the nasal and buccal mucous membranes, which give rise to repeated profuse hemorrhages either spontaneously or as a result of trauma. The vascular dilatations begin early in childhood and persist through life, individual lesions growing to the size of a split-pea. A profound anemia results from the repeated hemorrhages. Males and females alike are affected and the disease may be transmitted through three generations. There is no tendency to hemophilia in these cases nor is the coagulation time of the blood delayed.

Treatment.—Telangiectases are most successfully removed by electrolysis. In the case of the spider angioma the needle is inserted in the center of the lesion and a current of one to two milliamperes turned on for a few seconds until the area becomes white. A fine pointed cone of carbon-doxid snow can also be used under moderate pressure to obliterate the vessels.

Angioma Serpiginosum.—Definition.—A rare type of angioma beginning early in life and characterized by the formation of vascular puncta which spread peripherally, undergoing central involution, and giving rise to a serpiginous outline. The disease was described by Hutchinson as infective angioma or nevus lupus.

Symptomatology.—The disease begins insidiously on any part of the body by the formation of bright red or purple dots or papules, resembling grains of cayenne pepper, which spread out forming serpiginous outlines. In addition there may be present areas of diffuse, uniform redness, delicate vascular rings, meshworks of irregularly curved and crooked vascular lines, pigmented lesions, and atrophic spots (Wise). The malady is slowly progressive, new satellite spots developing which later coalesce. Subjective symptoms are absent and there is no tendency to hemorrhages. The general health is not affected.

Etiology and Pathology.—Of the 30 reported cases 16 began between infancy and the age of 10. In five cases a congenital vascular nevus was the starting point. Hyde and Montgomery report an infant in whom a congenital nevus of the vulva was the point of origin. In other cases the condition arises without a pre-existing lesion of the skin. Histologically Pollitzer found a low grade inflammatory process affecting primarily the capillary areas of the papillary and subpapillary regions with secondary effects in the epidermis.

Diagnosis.—Angioma serpiginosum, according to Wise, is a disease entity which differs from other dermatoses characterized by multiple telangiectases. It has a certain similarity to the condition known as purpura annularis telangiectodes (Majocchi) which begins in childhood with the formation of annular purpuric patches on the lower extremities chiefly. By some authors the two conditions are considered identical.

Treatment.—Treatment has no influence in arresting the progress of the disease. Localized areas may be improved by freezing with carbon-dioxid snow,. by electrolysis or with quartz light.

Granuloma Pyogenicum.—Definition.—A pedunculated tumor composed of granulation tissue developing at the site of a trauma probably as a result of infection with the *Staphylococcus aureus.* The disease was first described by Poncet, and Doré in 1897 as *botryomycosis hominis* and considered analogous to the botryomycosis of cattle. Subsequent investigations by Bodin, Wile, Heuk, and othere have shown that the suspected botryomycetes were clusters of staphylococci. The condition has also been labelled *granuloma telangiectodes* but is usually referred to as *granuloma pyogenicum* by American authors.

Symptomatology.—A pea to cherry-sized, purplish-red, pedunculated tumor rapidly develops in the skin at the site of an injury or wound. The tumor is round or slightly lobulated, resembling a mushroom with a short pedicle around which the surrounding epidermis often folds up like a collarette. The surface is smooth, moist, with a seropurulent secretion, often ulcerated and bleeds easily. There is a marked tendency to recurrence after removal, unless the base has been thoroughly cauterized. The growths have been observed chiefly in places exposed to injury, on the hands and feet, but may develop any where. The lips, chin, cheeks, scalp, arms, scrotum and in one of the author's cases the eyelids were affected. Fifty per cent. of the cases occur in middle life and only about 5 per cent. in children under 10. The youngest case on record is Wile's, a child of two months with a lesion on the navel. The author recently saw a child of 10 months with a pea-sized granulomatous lesion on the cheek which had been bleeding for several weeks.

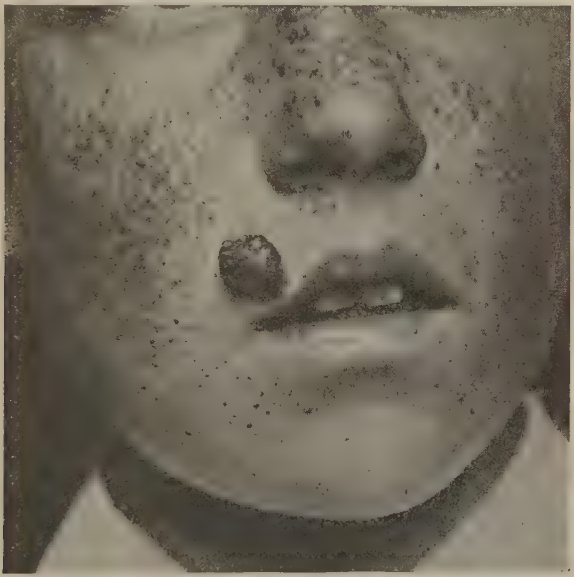

Fig. 62.—Granuloma pyogenicum. Duration 3 months. Developed at site of mosquito bite. (Collection of Dr. Grover W. Wende.)

Etiology and Pathology.—The etiologic factor is in all probability the *Staphylococcus aureus* which has been recovered in pure culture from the lesions and has been demonstrated in sections as clusters scattered throughout the tumor. The histologic picture resembles that of granulation tissue with newly formed connective-tissue cells and dilated vascular spaces showing endothelial proliferation. In extreme cases the vascular dilatation is so marked as to resemble that of an angioma. In addition there is a diffuse infiltration with connective tissue cells, polynuclear leukocytes and a few plasma and mast cells.

Diagnosis.—A reddish, rapidly growing pedunculated tumor which bleeds easily and springs up at the site of an injury gives a characteristic clinical picture. Nevertheless the tumor has frequently been mistaken for an angiosarcoma. The purely local character, the absence of infiltration at the base and the histologic structure excludes a sarcoma.

Prognosis and Treatment.—Granuloma pyogenicum is a benign tumor but persists unless properly treated. The tumor should be excised and the base thoroughly cauterized with nitrate of silver or carbon-dioxid snow.

Molluscum Contagiosum.—**Definition.**—A contagious disease of the skin occurring chiefly in children, characterized by the formation of small semi-globular tumors with a central depression. This interesting disease has been described in the literature under various names. Bateman first used the title molluscum contagiosum in 1817; later Bazin called it acnè varioliforme and Unna and Neisser described it as epithelioma contagiosum.

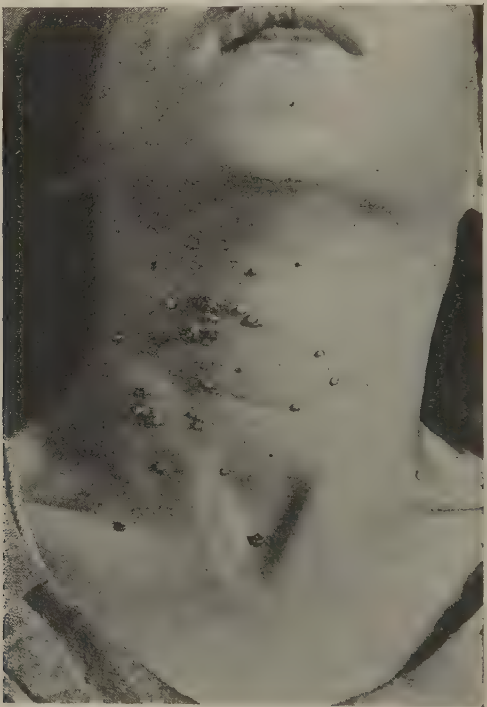

Fig. 63.—Molluscum contagiosum. (Fordyce and MacKee.)

Symptomatology.—Typical molluscum lesions appear as pinhead to pea-sized, semi-globular growths with a central depression. Their color is whitish or pink, with a peculiar waxy translucence which has been compared to that of mother-of-pearl. By pressure a cheesy-looking material is expressed or the entire contents can be shelled out as a firm, white lobulated mass leaving a bleeding cavity. This peculiarity formerly lead to the erroneous belief that the growths were connected with the sebaceous glands. In children the tumors are as a rule not much larger than a split-pea, although in rare instances much larger, pedunculated tumors have occurred. They are discrete or grouped and commonly localized about the face, especially the eyelids, neck, scalp, chest and hands. In adults the genitalia are a favorite location. In the average case not over a dozen lesions are present but occasionally hundreds are scattered over the face and body as Kaposi has seen. They grow slowly, may persist for many months, and either disappear spontaneously or are rubbed off mechanically. Suppuration is rare and subjective symptoms are usually absent.

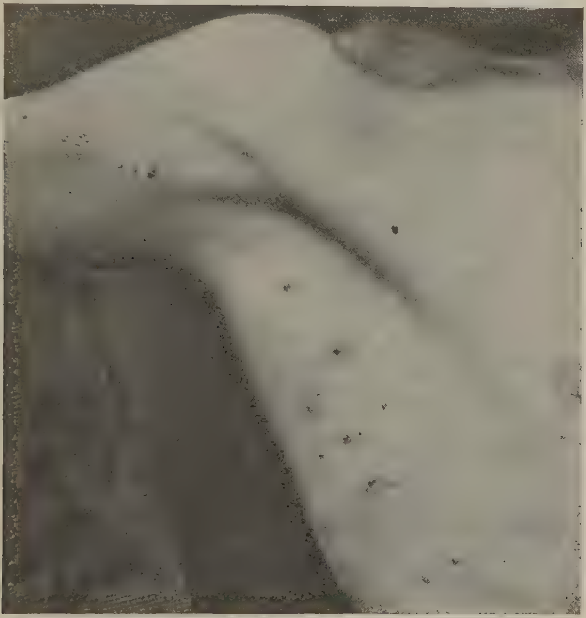

Fig. 64.—Molluscum contagiosum.

Etiology.—Molluscum tumors have been observed at all ages, although most commonly in children of the poorer classes. The disease has at the present time been definitely proved to be inoculable and contagious. The clinical and experimental evidence of the contagiousness has been presented by the investigations of Stelwagon, Jackson, Kaposi, Pick, Knowles, Allen, Fox and others. Instances of direct contagion have been abundantly observed in schools, institutions, bathing establishments and in families. Knowles collected 35 reports of family epidemics. The mother has been known to transmit the disease from the breast to the face of the nursing child. Accidental inoculations have occurred in physicians. Successful inoculation with the contents of the tumors have been reported by

Vidal, Retzius, Haab, Wile and others. The inoculation is not always easy and it is necessary to rub the material into the scarified or punctured skin. The period of incubation varies from 6 to 12 weeks or even longer. Juliusberg has successfully inoculated individuals from a filtrate, while Serra also found that the virus passes through a Berkfeld filter. Wile and Kingery in a recent series of experiments have also shown that the disease is caused by a filterable virus.

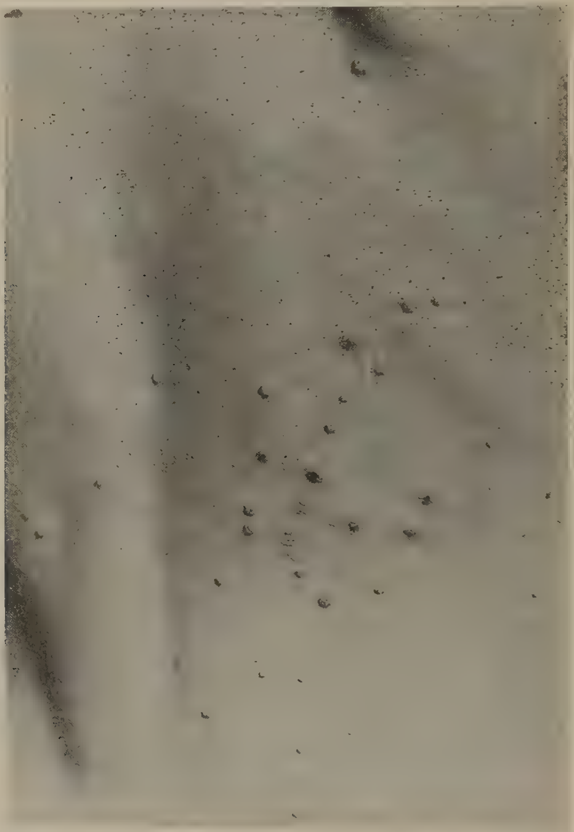

Fig. 65.—Molluscum contagiosum. (Ormsby and Mitchell.)

The actual cause of molluscum contagiosum is unknown, although undoubtedly a microörganism is responsible. White and Robey in 1902 made numerous attempts to cultivate organisms from the tumors without conclusive results. More recently Campana has described a sporozoon which he considers the etiologic factor. Lipschütz found peculiar minute stainable diplococcoid bodies which he called strongyloplasma and which he believed to be the actual virus. These observations have not been confirmed. An interesting fact is that pigeons and fowls suffer from a similar inoculable disease called epithelioma contagiosum of birds.

Pathology.—The histopathologic studies of Virchow, Neisser, Boeck, Crocker, Fordyce and Gilchrist among others have established the fact that molluscum contagiosum is a benign epithelioma with its origin in the prickle cells of the rete and is not a disease of the sebaceous glands as was formerly supposed. The rapid proliferation of the rete cells results in the formation of a lobulated mass surrounded by a fibrous capsule and divided by fine fibrous septa into individual lobules which open into a common central cavity. Each lobule is lined by a layer of tall palisade cells over which are several layers of practically unchanged epithelial cells. Above, the cells become rapidly transformed into homogeneous, oval hyaline bodies, with flattened nuclei, the so-called "molluscum bodies or corpuscles." Although originally regarded as protozoa developing in the cells and forming the basis of the psorosperm theory, these molluscum bodies are now known to represent degenerated epithelial cells which have become transformed into masses of keratin. In older tumors the cells at the neck of the central cavity become converted into a cheesy mass while the epidermis over the projecting part of the tumor gives way resulting in the umbilication. Recent studies by Wile and Kingery have shown the development of experimental lesions of molluscum contagiosum to be limited

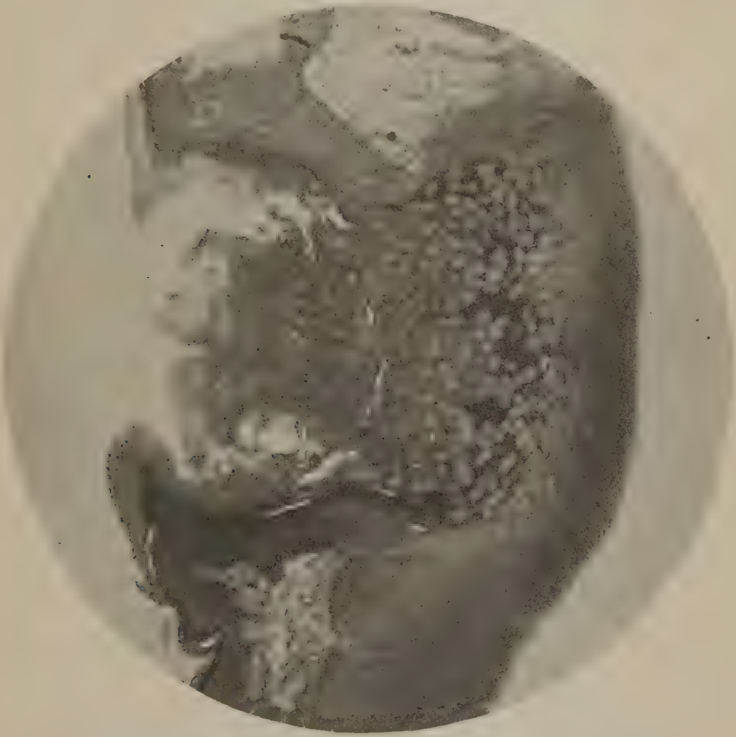

FIG. 66.—Molluscum contagiosum (moderate magnification).

to pilosebaceous epithelium and have again thrown open the question of the exact origin of the pathologic process.

Diagnosis.—The peculiar "mother-of-pearl" tumors are so characteristic that they can hardly be mistaken for other tumors. In children, especially, warts and milia should be differentiated. The microscopic picture in doubtful cases would at once settle the diagnosis.

Prognosis.—The disease is always benign.

Treatment.—The tumors may be squeezed out by lateral pressure with the fingers or the contents may be evacuated through a minute incision over the projecting part and the base touched with tincture of iodin or the nitrate of silver stick. Healing is rapid. A mild antiseptic lotion is used to prevent recurrence and the development of new growths.

Sarcoma Cutis.—**Definition.**—Sarcoma of the skin may be classified as (1) non-pigmented sarcoma, either solitary or multiple; (2) pigmented sarcoma; (3) multiple pigmented hemorrhagic sarcoma (Kaposi). In contradistinction to carcinoma of the skin, which is primarily a disease of advanced age, sarcoma of the skin may occur at any age.

Symptomatology.—**Solitary Non-pigmented Sarcoma Cutis.**—A primary sarcoma of the skin may be a congenital new growth or may develop in the first few years of life either in the normal cutis as a result of trauma or at the site of a pre-existing scar, nevus or fibroma. Cases of solitary sarcoma occurring in infancy have been reported by Jacobi and others. The malignancy depends upon the type of cell present. The fibrosarcoma begins as a hard white or pink movable nodule which grows slowly, seldom metastasizes, and is curable by early excision. The spindle-cell sarcoma forms a variously colored plate-like nodule, varying in size from a pea to an egg, situated in the corium or subcutaneous tissue. Further growth results in either a hard node or a soft fungating tumor. Secondary nodules may appear in the skin, subcutaneous tissue, glands and internal organs after a variable period. The round-cell sarcoma begins as a bluish-red vascular nodule in the apparently healthy skin or by the breaking down of a nevus. This is the most malignant form which ulcerates and metastasizes rapidly. An isolated giant-cell sarcoma of the skin is extremely rare although cases have been described by Unna, Pasini, and Zeisler. Rahel-Zipkin reported a sarcoma of the groin in an 18 months old boy with a polymorphous structure showing giant cells of the Langhans type.

Multiple Non-pigmented Sarcoma Cutis.—In this type there are present disseminated cutaneous or subcutaneous tumors of varying size of a pink or a reddish-blue color. Individual nodules may grow to the size of a hen's egg, break down and ulcerate. Metastases take place by the way of the blood stream chiefly. The cases terminate fatally in a few months or a year. Most of the tumors are of the spindle or round-cell variety. Odstrĉil, however, described a rare case of primary multiple giant-cell sarcoma of the skin with metastases in the inner organs in a six months old child. Dubreuil has personally observed five cases of infantile sarcomatosis at ages varying from one month to six years. Other instances of congenital sarcomatosis have been reported by Neuhaus, Karewski, Johnston, Pernet, De Beurmaun and Gougerot, Perera and others. Cutaneous sarcomas secondary to visceral sarcoma particularly of the kidney, testicle, or lymph glands have also been observed in infancy (Ramdohr). It is possible that some of the cases reported as true sarcomatosis have been multiple tumors of the skin occurring in leukemia or pseudoleukemia.

Multiple Pigmented Hemorrhagic Sarcoma of Kaposi.—This is a disease of adult males chiefly, presenting as infiltrated purplish vascular plaques on the lower extremities. Cases beginning in early life according to Morris have been observed by De Amicis (five years) and by Corlett (two years).

Melanoma.—The most important feature of the melanotic neoplasms is that they originate in congenital moles or pigmented warts which have been subjected to irritation or trauma. The usual history is that a pigmented mole, which may have been present for many years, begins to ulcerate, becomes indurated at the base and increased in size. Within a short time the regional glands enlarge and may break down. In other cases large numbers of gray or black, pea to nut-sized nodules appear in the subcutis scattered over the body. Visceral metastases are most frequent in the lungs, liver, spleen, kidneys, and brain. The primary tumor may be a black spot on the foot (malignant lentigo), in the matrix of the nail (melanotic whitlow), in the pigmented structures of the eye and occasionally in the rectum or lymphatic system. In many cases the primary tumor is an insignificant lesion. The duration of life in the average case is not over six months or a year; rarely longer. Melanomas occur most frequently after the age of 40 and are extremely rare in early life. Juvenile cases have been reported by Coley (melanoma of the eye in a child of 1½ years), Battle (child of three months), Magyar (one year), and others. Netherton recently reported a case of malignant melanoma of the lower lip in a child, the growth of which was temporarily controlled by radium. The chief lesson to be drawn from these extremely malignant tumors is that prevention is better than cure. Every congenital or acquired mole, particularly if it is exposed to irritation, should be removed in early life preferably by the knife or cautery.

Etiology.—The cause of sarcoma is obscure. Recent studies on the cultivation of sarcoma cells in vitro and on the growth of fowl sarcoma have supplied many interesting data, but have not cleared up the etiology. Leyton believes the active cause of sarcoma is a streptothrix the spores of which pass through a Chamberland filter. He has successfully inoculated rats with an emulsion of rat sarcoma passed through a Berkefeld filter. Melanotic tumors in man have been successfully reproduced by inoculation under the skin of animals (Becheaux, Goujon). The most important point in the etiology is that non-pigmented sarcomas rarely begin in the normal skin but usually originate in some pre-existing benign lesion as a congenital nevus, scar, or fibroma. The melanomas develop from pigmented moles probably as a result of trauma and irritation. Heredity plays a doubtful rôle. Age and sex are of no importance.

Pathology.—The non-pigmented sarcomas are composed chiefly of large or small, round or spindle cells in a vascular stroma. The cells at times present an alveolar arrangement. When the fibrous structure is pronounced, the term fibrosarcoma is used and the tumors which originate apparently from the adventitia of the blood-vessels are termed angiosarcoma. The melanomas are composed of a matrix of spindle, less often round cells with excessive amounts of a black pigment called melanin. Müller, Unna, and Krompecher believe in the epiblastic origin of nevi and therefore look upon melanotic tumors as carcinomas. Virchow, Ribbert, Handley, and Adami believe in the mesodermic origin of the nevoid cells and therefore regard these cases as melanotic sarcoma. Johnston believes that nevi are of endothelial origin and Fordyce holds that melanomas may have a twofold origin either from the basal cells of the epidermis or from the endothelium.

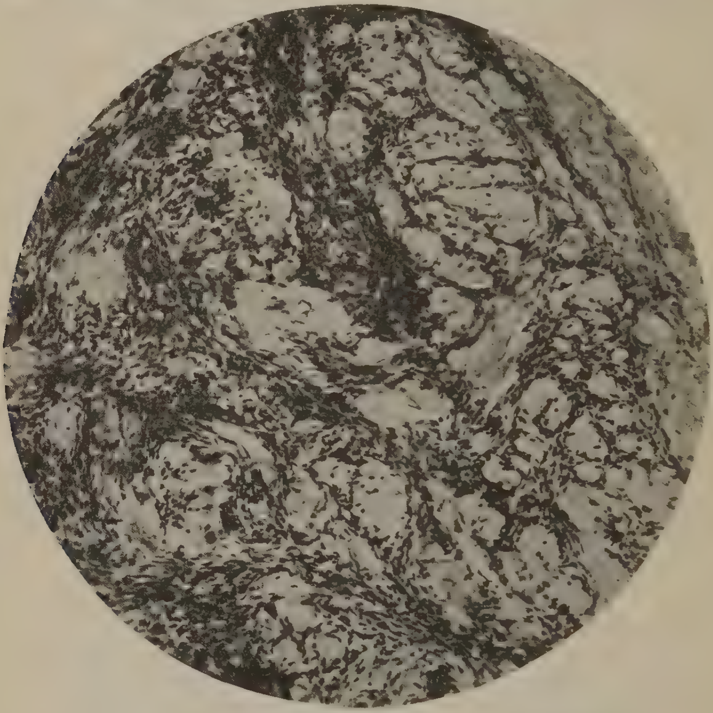

FIG. 67.—Spindle-cell sarcoma—moderate magnification.

The multiple pigmented hemorrhagic sarcoma of Kaposi presents histologically large cavities filled with blood between which are parallel rows of spindle cells with pigment deposit. Gilchrist and Ketron believe that the skin lesions begin as angiomata, followed by connective tissue and endothelial proliferation which obliterates the blood spaces forming solid tumors. The condition has been variously considered as a sarcoma, a granuloma, and a chronic inflammatory process.

Prognosis.—The prognosis depends chiefly on the type of cell. The solitary spindle-cell growths are curable by early excision. The round-cell forms are extremely malignant. The disseminated and melanotic varieties are fatal in a short time. On the other hand, the Kaposi type often lasts many years.

Diagnosis.—Sarcomas are differentiated from benign tumors by their more rapid growth. A microscopic examination may be necessary to establish the diagnosis.

Treatment.—Solitary sarcomas should be excised at the earliest possible time in order to prevent dissemination. Radium or *x*-ray may be used subsequently as prophylactic measures. In the multiple sarcomas treatment is of no avail. Recourse must be had to large doses of arsenic, Coley's serum and general supportive measures. The cases of sarcomatosis reported as cured by various authors were probably examples of multiple sarcoid tumors, which respond to the administration of arsenic. The best treatment of melanotic growths is prevention. All pigmented spots or warts exposed to irritation or showing a tendency to growth should be excised at once. Advanced melanomas should be treated by radical excision with subsequent radiotherapy. Even early interference, however, will not always prevent metastases. Coley has reported a favorable action from his serum in a few cases.

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CLASS VII. DISEASES OF THE APPENDAGES OF THE SKIN

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(A) Diseases of the Coil Glands

Hyperidrosis.—**Synonyms.**—Hyperhidrosis, Sudatoria, Idrosis, Hydrosis, Ephidrosis, Polydrosis.

Hyperidrosis may be general or local. The generalized form is of interest mainly to the internist, because it is a common symptom of febrile disease and of some of the nutritional and nervous diseases. The idiopathic generalized form and the localized varieties concern the dermatologist and the neurologist. The parts in which the sweat glands are most highly developed, the scalp, face, axillæ, palms, soles and the genito-crural region, are the ones usuallly involved.

Symptoms.—A common example of this disorder is the "Hyperidrosis nudorum" of patients exposed for examination in the clinic. The excitement causes rivulets of sweat to trickle down from the axillæ. Others have hands that are always cold and damp, or that drip sweat within a few minutes of having been wiped dry. The constant moisture makes the parts more susceptible to injury from cold, trauma and infection. Furunculosis, folliculitis, miliara rubra, intertrigo and certain fungus diseases are therefore common complications. Eczematoid ringworm finds a favorable soil upon palms and soles kept moist by excessive sweating, and hyperkeratoses may result from the ringworm infection or as an accompaniment of the abnormal condition of the coil glands.

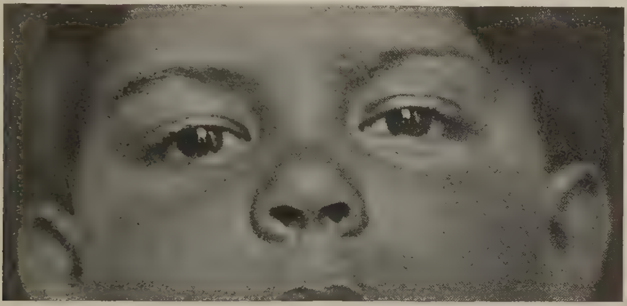

Fig. 68.—Localized hyperidrosis. (Collection of Dr. R. L. Sutton.)

Sharply circumscribed hyperidrosis makes a striking picture. Sutton's case of the boy with an area of hyperidrosis 5 cm. in diameter in one eyebrow is a good illustration. Any part may be affected to any extent, even to half the face or half the body. The rest of the skin may be normal or anidrotic.

Etiology.—Both sexes and all ages are affected; but the disease is commoner in youth. Congenital cases are recorded. Nervous instability is the most frequent cause, and it may be secondary to infections like malaria, or to the toxic action of intestinal products or the use of tea, coffee, alcohol, or tobacco. Nervous explosions like migraine and epilepsy may be manifested by local hyperidrosis. Rare cases are reported in which the odor or taste of certain foods excited localized hyperidrosis, although the skin of the involved area reacted normally to ordinary stimuli. Torök's case is a noteworthy example. Heat, warm drinks and exertion caused sweating of the right side of the face, neck and chest, while the taste of cayenne pepper, vinegar, cheese or mustard caused the left side to perspire.

Hyperidrosis of the scalp may be symptomatic, as in rickets, or idiopathic. It is often part of the picture of seborrhea, and when the sweating is the most striking symptom the condition is known as oily hyperidrosis. Passive congestion of the hands and feet is often associated with hyperidrosis of these parts, and may be causative. Vicarious hyperidrosis occurs in cases in which the greater part of the skin is anidrotic, as in ichthyosis, and it is not uncommon for patients to claim that as axillary hyperidrosis yields to treatment, increased sweating occurs in other places.

The sharply circumscribed variety may be caused by irritation of nerve trunks by tumors, injuries or scar formation. Pressure on the plantar nerve as a result of flat foot is frequently cited as a cause of excessive sweating of the feet. Herpes zoster has been followed by sharply circumscribed hyperidrosis in the area of the affected nerve, and enlarged cervical glands sometimes cause unilateral sweating of the face by pressure on the cervical sympathetic.

Pathology.—Histologic examination, according to Robinson, has shown no anatomical change in the skin or its appendages, while Sutton records hypertrophy of the coil glands, dilated blood-vessels and cellular proliferation about them.

Treatment.—Generalized hyperidrosis is best treated by efforts to remove its cause. When this is not possible, tonics as iron, arsenic and quinin are recommended, and for direct lessening of the perspiration atropin hypodermically, of course with great caution and usually with only a temporary effect. In the localized cases, the cause should be treated if this is possible. Aluminum chlorid, 25 per cent. in distilled water, dabbed on the part once every third day and allowed to dry on, is very efficient. Care must be observed that no alkali, such as soap remaining on the skin, is allowed to neutralize it. Too frequent use, or scratching after its use, may cause a dermatitis, and in children response by scratching to the stinging sensation sometimes caused by the drug may be hard to avoid. Usually a few applications will give relief for some time, so that its use may be suspended until the trouble recurs.

X-rays from a hard tube given cautiously, always keeping below the erythema dose, is a very efficient remedy. One series of exposures may give lasting relief; but many cases recur and require a repetition. Some relief can be gotten from a lotion of 50 per cent. alcohol with 1 or 2 per cent. salicylic acid. Tannic acid or zinc sulphate from 1 to 16 per cent. are also recommended.

Anidrosis.—**Definition.**—Anidrosis is a condition in which no sweat is secreted. Most of the cases are more correctly oligidrosis or hypohidrosis. It may be local or general. Three cases of complete anidrosis have been reported by Taendler, Wechselmann and Loewy. All were girls of the same family, and in addition to the lack of sweat glands the hair was sparse, only a few upper teeth were present and no lower teeth. One lacked breasts and nipples.

Etiology.—Congenital anidrosis is usually associated with ichthyosis, and is only partial. By increasing evaporation, febrile conditions may cause an apparent lessening of perspiration, and the same effect may be produced by chronic scaly eczema, psoriasis or pityriasis rubra pilaris by increase of the evaporating surface. The skin of these patients secretes normally after the disease is cured. Diuresis, in diabetes mellitus or insipidus or in chronic nephritis, may cause oligidrosis, or the same effect might be due to severe diarrhea. Localized anidrosis may be caused by destruction of the glands by scars or scleroderma, or it may follow any of the nerve lesions mentioned as causing hyperidrosis.

Treatment.—Treatment of the underlying cause, when this can be ascertained, is the important indication. Hot baths and increased water drinking may be helpful, and if necessary, pilocarpin may be tried with caution.

Bromidrosis.—Synonym.—Osmidrosis.

Malodorous sweating is due either to secretion of sweat containing an evil smelling constituent, or to decomposition of the sweat after it has been secreted. It is usually associated with localized hyperidrosis; but a generalized form occurs in diabetes, typhoid, typhus, Asiatic cholera, dysentery scurvy, septicemia and pyemia. It is due to absorption of the products of abnormal gastro-intestinal metabolism, or to waste matter excreted by the skin, as in the uridrosis of uremia. Some ingested substances as asafetida, valerian, sulphur, benzoic acid, copaiba, onions, garlic and musk may impart to the sweat a characteristic odor. Personal and racial peculiarity as to the odor of the sweat is a well-known fact, and it may be that this should sometimes be classed as mild bromidrosis.

Bromidrosis of the feet is by far the commonest form of the disease and is due to decomposition of the sweat by the *Bacterium fetidum* of Thin, one of the soil bacteria. The localized form of the disease occurs also in the axilla and the ano-genital region, where it is often associated with intertrigo. In chronic alcoholism, gout, excessive use of meat and in constipation, as in the diseases above mentioned, intestinal absorption may be the source of the odorous substance. This may also be true of the cases of hysteria and neurasthenia in which the sweat has a bad odor. Cases have been reported in which the sweat had the odor of violets or pineapple.

Treatment.—For generalized bromidrosis the underlying cause should, if possible, be removed. Regulation of the diet and increase of bowel action will benefit some cases. Sodium salicylate in moderate dosage has been sucessful in some cases, phenol or alkalies in others. The localized forms are usually relieved by treatment of the excessive sweating. Aluminum chlorid or *x*-rays will control most of them. If necessary, foot baths of potassium permanganate, solution 1:500 to 1:100, may be used every night. A generous use of boric dusting powder in the socks and shoes is helpful.

Chromidrosis.—Chromidrosis (colored sweat) is always localized, most often on the face, especially the lower eyelid, sometimes on the neck, back or chest, hands, axillæ or genito-crural region. A number of cases in children have been reported. It usually occurs in constipated, neurotic subjects, and is related to the still rarer cases of colored vomitus, urine, feces and milk. In most cases the color is due to the oxidation of some excreted substances as indigo or iron salts, but in others the pigment is thought to have been produced by growth of bacteria. Darier refers to R. Blanchard's case of a 13 year old boy upon whose eyelids an adherent black substance similar to choroidal pigment was found about the sweat ducts. Green or bluish sweating has occurred from absorbed copper.

Pseudo-chromidrosis is a fairly common disorder due to the growth of a fungus, lepothrix, with or without associated bacteria, on the hair of the axilla or scrotum. The color is usually yellow or reddish-yellow or brown; but other colors are seen occasionally. Not in uncommonly only one axilla is affected, and cases are recorded which the colors were different in the two axillæ. In the common variety, the underwear is stained bright yellowish-red. The deposits along the hair shaft, with swelling and sometimes fracture of the hair, make the diagnosis easy.

In cases purporting to be true chromidrosis the possibility of stains applied by a neurotic patient to arouse interest should always be kept in mind.

Treatment.—The pigment of true chromidrosis can be removed with ether, alcohol or chloroform. If discoverable, the underlying condition should be treated. The condition, which is so often due to constipation, readily yields to treatment; but not seldom recurs.

False chromidrosis due to lepothrix yields readily to antiseptics and anhidrotics. An alcoholic lotion containing bichlorid of mercury 1:1000 or 1:500 is recommended. Hartzell says that shaving of the part is necessary to a cure with subsequent applications of the lotion.

Hematidrosis.—Synonym.—Bloody sweat.

This very rare disorder occurs usually in women; but mention is made in the literature of cases in the newborn and in hemophilic children. It is due to hemorrhage into the sweat glands, the blood, diluted with sweat, appearing on the surface of the unbroken skin at the duct orifices. On removing it, another drop exudes. This demonstration is necessary to a diagnosis, for most of the cases reported as hematidrosis occur in hysterical subjects to whom deception is a fine art. The phenomenon lasts usually for only a few minutes at a time, but sometimes for hours. Purpura and internal hemorrhages may be associated. Treatment must be directed to the cause, hemophilia or nervous disease.

Uridrosis.—A rare phenomenon, occurring in the uremia of yellow fever or, less often, in nephritis. A silvery deposit of urea appears on the skin of the eyebrows or scalp, sometimes on the neck, breast, axilla or extremities. Riecke mentions exceptional cases in which it has been seen on the mucous membranes of the mouth and pharynx.

Sudamen.—Synonyms.—Sudamina. Miliaria crystallina. An eruption of clear vesicles up to pinhead size, upon a skin of normal color. It is caused by occlusion of sweat ducts by the cells of the stratum corneum, and the accumulation of sweat under or within this layer. The rapid evaporation of sweat during the febrile stage of the acute fevers affords opportunity for the partial occlusion of the duct orifices, which are then too small to handle the flood of sweat during defervescence. Or, as Pollitzer suggests, horn cells deficient in oil become swollen by inhibition and block the mouth of the duct. The vesicles thus formed usually remain for hours or even days, and their spontaneous disappearance is followed for a day or two by scanty fine desquamation. Any sudden onset of hyperidroses is apt to be followed by such an eruption.

The diagnosis is made upon an eruption of minute clear vesicles upon a non-inflamed skin, following an attack of sweating. The absence of albumin in the contents of the vesicles might be of diagnostic value to differentiate from inflammatory dermatitis.

Treatment.—The only treatment needed is to prevent recurrences. Cooler clothing and a dusting powder usually suffice. If hyperidrosis persists, it should be treated as suggested under that heading.

Miliaria Rubra.—Synonyms.—Prickly heat. Heat rash. Lichen tropicus. Strophulus. Red gum.

A mild, diffuse inflammation of the skin following a severe attack of sweating, characterized by a thickly set eruption of discrete papules (M. papulosa) or vesicles (M. vesiculosa) on an erythematous base, accompanied by itching or a burning sensation. The lesions seldom exceed pinhead size, and seldom become confluent. The vesicles, like those of sudamen, do not rupture easily, but dry up and desquamate. Before resolution the contents of some of the vesicles become cloudy (M. alba). Nearly always both types of lesions are present, the vesicular usually predominating.

An attack lasts from a few days to two weeks; but may last longer if the cause cannot be relieved. Relapses are common. The back and chest, the flexor surfaces of the limbs and the folds of the body are usually affected, and newborn infants, debilitated or overfat children are most liable to the disease. Any of the complications of hyperidrosis may occur with miliaria rubra, most commonly intertrigo or abscess of the sweat follicles.

Etiology and Pathology.—The general opinion of dermatologists has been that miliaria rubra is the result of the factors causing sudamen plus an irritation which results in the inflammatory reaction. Darier believes it a miliary impetigo.

Diagnosis.—From sudamen, miliaria rubra is differentiated by the inflammatory feature. From papulo-vesicular eczema, the absence of grouping or confluence of the lesions at the center of such groups, distinguishes it. The itching is less than in so acute an eczema, and in the latter the vesicles are much more fragile. The sudden onset of miliaria after sweating, and the prompt response to treatment also differentiate.

Treatment.—Salicylic lotion, 0.5 per cent. in 50 per cent. alcohol, is very effective. This may be used after the bath or in place of it.

Calamine lotion, calamine powder and zinc oxid, āā 16.0 to 240.0 of lime-water, may be dabbed on and allowed to dry. Removal of the cause, as excessive clothing, is necessary. Sponging with dilute alcohol is valuable to prevent recurrence, as is the generous use of dusting powder.

Granulosis Rubra Nasi.—A rare disease, first described by Luithlen in 1900, occurring in children and usually clearing up about puberty; but sometimes persisting, as in Pinkus' case, throughout life. Associated with localized hyperidrosis are seen small, sharply defined, bright to dark bluish or brownish red papules on the tip and alæ of the nose, and sometimes on the upper lip and chin or cheeks. The skin between the papules is usually bluish and cold and similar signs of passive congestion are often found in the hands and feet. It occurs in poorly developed children, and has been seen in several of the same family. With it is often associated hydrocystoma, which Jadassohn considers a sequel of the granulosis. The lesions may be infected and form pustules, but do not ulcerate.

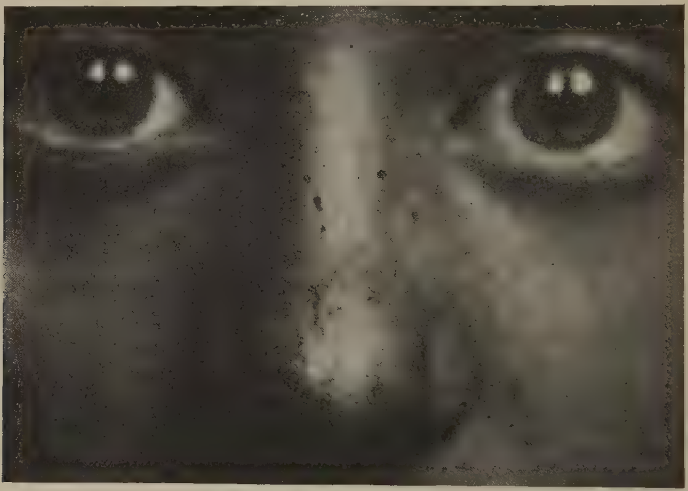

Fig. 69.—Granulosis rubra nasi. (Collection of Dr. J. E. Lane.)

Etiology.—Poor circulation, dependent on some general deficiency, is responsible; but upon just what the circulatory defect depends, and whether it is the sole cause, is not known. Histologically the blood-vessels of the corium are dilated, and about them and the sweat glands there is an infiltration of polymorphonuclears, connective tissue cells, and a few plasma and mast cells. Cysts of the sweat ducts are often present. The sebaceous glands are not involved.

Diagnosis.—From rosacea, youth and localized sweating with absence of dilated arterioles and venules distinguish it. Sweating and hydrocystoma are prominent in granulosis, and the papules are more numerous, more sharply defined, more sharply localized, and more persistent than in rosacea. Lupus vulgaris papules show brown and translucent under the diascope, while granulosis papules disappear. There is no infiltration, ulceration or scarring in granulosis and the lesions are fairly symmetrical, while the opposite is true of lupus vulgaris. The papules of acnitis often show a translucent brown under the diascope, are more widely distributed, often leave scars and lack the bluish color, the sweating and the great chronicity of granulosis rubra nasi.

Treatment.—The child should be kept out of doors and the general condition improved by wiser feeding, regulation of habits and better hygiene. Tonics or cod-liver oil may be useful. Locally, astringent powders, as tannoform, 25 to 50 per cent., are recommended. Pusey and Sutton suggest *x*-ray therapy as indicated theoretically, and Winfield reports a case in which it was of temporary benefit, as was also the high frequency current. Recurrences in his case were caused by dietary indiscretions.

(B) Diseases of the Sebaceous Glands

Seborrhea.—**Synonyms.**—Seborrhea oleosa. Stearrhea. Seborrhagia. Fluxus sebaceus. Hyperidrosis oleosa.

The sebaceous glands are active before birth, discharging their product upon the skin of the infant, where it dries soon after birth, forming the vernix caseosa, a mixture of sebum, epidermal scales and lanugo hair which soon separate in large flakes, leaving the skin normal. During childhood excessive sebaceous activity is rare, becoming common after puberty, and again decreasing to below normal in old age.

A tendency to oily skin, with large pores, is often hereditary, but as has been said, seldom becomes manifest in childhood. The nose is the center of such abnormal activity, and the greasy appearance of the face is often much more noticeable than that of the scalp, where the oil is distributed on the hair. Seborrhea is often associated with hyperidrosis; but Unna's claim that the sweat glands supply the greater part of the fats is not upheld, though it is acknowledged that they produce a part.

Symptoms.—The skin of the face, especially about the nose, is shiny, and in severe cases may exude drops of oil. The scalp and hair also shine with excessive oil, and long hair may be matted with grease. Other portions of the skin may be involved especially in negroes, in whom the condition is much more common than in whites. The skin of the face appears coarse because of the dilated sebaceous ducts from which comedones can be expressed. The same phenomenon on the scalp has been made the diagnostic test for the disease by Sabouraud. Because of the ready adherence of dust and soot, the skin is difficult to keep clean. Hyperidrosis of face and scalp is often associated, and acne vulgaris, pityriasis capitis and dermatitis seborrheica are frequent complications.

As a result of long-continued seborrhea of the scalp, baldness occurs, beginning usually at the vertex by the growth of shorter finer hairs to replace the long ones, which are shed more rapidly than normal. The shorter hairs are in turn shed and replaced by still finer and shorter ones, until a diffuse bald area appears, gradually enlarging peripherally until only a fringe of hair is left at the sides and back of the scalp. The bald portion sometimes gives evidence of its origin in the shiny appearance due to excessive oil, though this is often replaced by hyperidrosis after the loss of the hair.

Etiology.—The disease occurs in either sex and at any age, more commonly at or after puberty than before. It affects brunettes more often than blondes. An hereditary tendency is often observed, and this, aided by malnutrition, especially that due to chronic intestinal disorders, permits the disease to start up. It must be confessed, however, that it not seldom occurs in persons apparently healthy in all other respects. It is claimed by Sabouraud that his microbacillus is the cause of the disease, but this claim is not yet generally acknowledged.

Pathology.—The dilated blood-vessels of the papillary layer are surrounded by an infiltration of leukocytes, plasma and mast cells. The sebaceous glands are greatly enlarged, the hair follicles decreased in length and breadth, and more than the normal number of hairs are seen in the bed-hair stage. The sebaceous ducts are dilated and filled by the comedones, or seborrheic filaments.

Diagnosis.—Increased oilness of the scalp and hair and the presence of seborrheic filaments with diffuse alopecia beginning at the vertex, are diagnostic. Scaliness of the scalp, if diffuse, indicates a complicating pityriasis, if localized with underlying redness, seborrheic dermatitis, which may sometimes be found also on the forehead, eyebrows, about the nose or on the trunk.

Prognosis.—The disease is very resistant to treatment and very likely to recur when energetic treatment ceases.

Treatment.—The general tone of the patient must be raised in every way possible. Local treatment consists of the application of ointments or lotions containing sulphur, resorcin or euresol pro capillis, some of the tars and salicylic acid in ointments or lotions. A very satisfactory lotion for greasy scalps is lotio alba; 4.0 grams each of sulphuretted potassium and zinc sulphate to 120.0 cc. of distilled water, to which resorcin, 4.0 grams, may be added. During intermissions in active treatment, alcoholic lotions containing 2 or 3 per cent. salicylic acid or 5 per cent. chloral hydrate may be used. The hair should be washed as often as the oilness demands. Vigorous brushing and other massage are to considered very important parts of the treatment. The hair brushes and combs should be washed frequently and then soaked in a formalin solution to prevent reinfection. Whatever treatment is employed, and it is advisable to change from one to another, persistence and constant vigilance are necessary to prevent recurrence. In times of lowered general resistance this vigilance should be increased.

Dermatitis Seborrheica.—**Synonyms.**—Eczema seborrheicum (Unna). Seborrhea corporis (Duhring).

Definition.—A disease of the skin characterized by sharply circumscribed patches of dermatitis covered by yellowish greasy scales, occurring most frequently on the scalp, face and mid-line of trunk.

Symptoms.—The first symptom is often moderate itching, calling attention to sharply defined patches of greasy scales, yellowish-white in color, easily removed, leaving a more or less reddened, very slightly elevated base. At times hardly any redness can be seen, and it is seldom very intense. In about half the cases the redness is more marked at the border of the lesion and often definite rings are formed by the clearing of the center of the patch. The lesions are usually 0.5 cm. or more in diameter, and are distributed on the scalp, just outside the hair line on forehead and neck, on the face especially in the eyebrows, in the nasal furrows and on the upper lip and ears. It occurs also on the chest and back especially in the mid-line, and less often in the axillæ, groins, about the umbilicus, on the ciliary borders of the eyelids, or generalized.

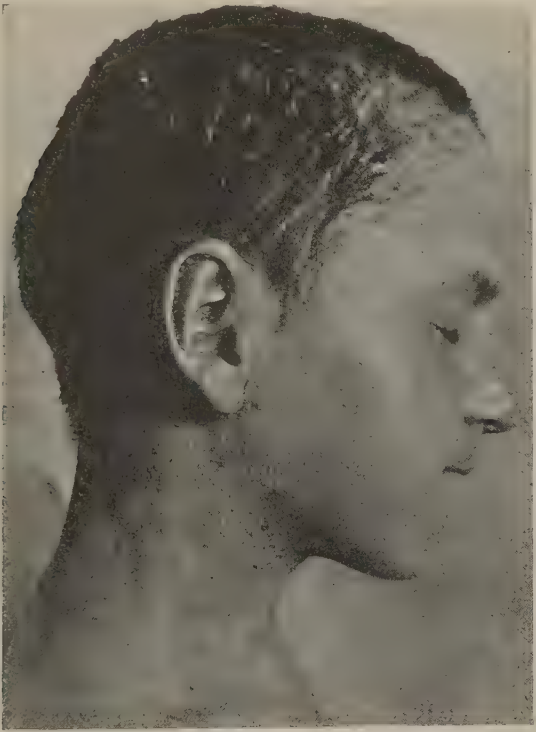

Fig. 70.—Dermatitis seborrheica. (Ormsby and Mitchell.)

On the glabrous skin the scales may lack the greasiness characteristic upon the scalp. The lesions are never moist except when macerated as in the axilla or groin, or where excoriated. They enlarge peripherally, like psoriasis papules, sometimes joining and producing large patches with gyrate borders.

Trimble has recently described a follicular form of this disease which is usually localized on the trunk, sometimes on the scalp and along the hair-line of forehead and temples, rarely on the face. The lesions are grouped but discrete dilatations of the mouths of the follicles, with surrounding redness and heaped up greasy scales "making a tiny cone." Less often a diffuse eruption of the same kind is seen over the upper half of the body, except the face. It is resistant to treatment.

Cheilitis exfoliativa, a very persistent disease of the lips characterized by adherent dry scales, is held by most dermatologists to be a form of seborrhoic dermatitis from the fact of its occurrence in patients with the latter disease, especially in neurotic women and in children.

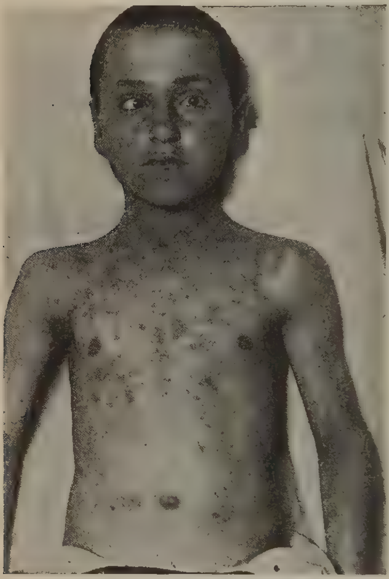

FIG. 71.—Dermatitis seborrheica. (Ormsby and Mitchell.)

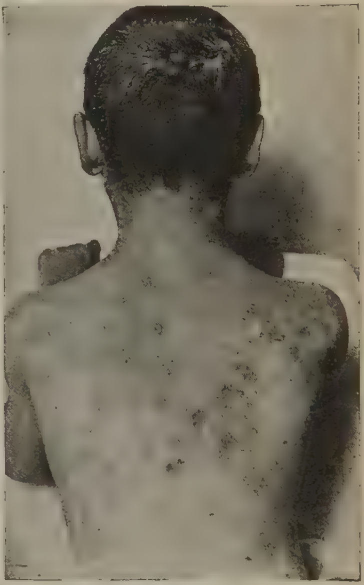

FIG. 72.—Dermatitis seborrheica. (Ormsby and Mitchell.)

Complications.—A tendency to seborrheic dermatitis is often excited by syphilis, and secondary or tertiary syphilids of the face or scalp may have a greasy appearance because of this fact. Acne vulgaris is often associated with seborrheic dermatitis; but this seldom leads to any confusion in diagnosis. Some of the earmarks of seborrheic dermatitis are commonly seen in infantile eczema. When in doubt, it is always safer to consider the case, at least at the beginning, as eczema, and treat conservatively.

Etiology.—It may occur at any age, and while constipation, gastro-intestinal disease, anemia, tuberculosis or other debilitating diseases predispose, it often occurs, without any discoverable predisposing cause, in individuals apparently normal except for the skin disorder. Locally, an oily seborrhea predisposes, if it is not the first sign of the disease. Uncleanliness of scalp and body increases the liability to infection or to recurrence. Lack of out door exercise also is a predisposing factor; but as already said, the disease occurs frequently without any of these factors.

Unna's claim that the disease is an infection is conceded by most authorities; but whether the causative organism is the spore of Malassez, the morococcus of Unna, the acne bacillus, or some undiscovered organism, is still in doubt. The infection is supposedly carried by combs and brushes, but only to those predisposed.

Pathology.—Histologically, the resemblance to eczema is striking. Parakeratosis, acanthosis and spongiosis are the main features, as in eczema, but the edema is not so marked, the vesicles are always microscopic in size, and the pathologic changes are often seen only at the border of the lesion. Darier distinguishes a psoriasiform type, in which acanthosis and scale formation is much more marked, while spongiosis is seen only here and there. The thinning of the rete mucosum over the tip of the papilla is not so marked as in psoriasis, nor is the acanthosis so regular. The infiltrate about the dilated blood-vessels of the papillary layer is composed mostly of connective tissue cells instead of the polymorphonuclear leukocytes so numerous in psoriasis.

Diagnosis.—The greasy character of the scales, upon sharply circumscribed dull or yellowish red maculo-papules, the characteristic distribution on the hairy parts, about the face and in the median line of the trunk, and the slight itching, make the typical case of this disease easy to recognize. The ease with which it yields to mild sulphur applications is also characteristic.

Psoriasis is distinguished by its typical distribution, favoring the extensor surfaces at the periphery, and usually avoiding the flexors and the genito-crural folds. The scales of psoriasis are dry and white, and may often by removed in a sheet, leaving a dark red macule covered by thin epidermis. Especially on the scalp do the scales of psoriasis tend to pile up, which is not true of the less numerous greasy yellowish scales of seborrhoic dermatitis. Neither does the latter attack the palms and nails, as psoriasis frequently does. Psoriasis is also much more resistant to treatment.

Eczema causes weeping, which is rarely true of uncomplicated seborrhoic dermatitis, the itching is more severe in eczema, and the patches are made up of minute lesions, confluent at the center and discrete at the periphery, producing a border which is not sharp, but fades into the normal skin. The mildest sulphur application may irritate an acute eczema, or there may be a history of irritation from soap or even from clear water. Scaly eczema usually is infiltrated and inelastic, and eczema patches never clear in the center.

Pityriasis rosea begins as a maculopapule without scales, the scales showing only on scratching the surface, and more at the center than at the borders of the older lesions. It almost never affects the scalp, and seldom the face, and runs a course of a few weeks, often beginning in an initial plaque, which precedes the generalized outbreak by a week or more.

Treatment.—Sulphur is the great remedy for seborrhoic dermatitis, as it is for other diseases of sebaceous origin. Applications of sulphur ointment, from 2 to 25 per cent., usually cause rapid disappearance of the itching and the lesions. The mild strengths should be used upon the face and body, the stronger on the scalp; but even here beginning with mild applications. Before application of the remedy the part may be washed with green soap and hot water. Macerated moist lesions in the axillæ or groins must first be treated with soothing, drying applications as calamine lotion, or zinc paste, before the use of the sulphur preparations is begun. As the lesions disappear, the ointment may be substituted by lotions, lotio alba or alcoholic lotions of salicylic acid, resorcin or bichlorid of mercury. Even alcohol alone is useful in preventing recurrences, as Pusey states.

Jadassohn recommends pyrogallol, 0.1 per cent. for the scalp, or 1:3000 chrysarobin zinc paste for the body. Trimble recommends acne bacillus vaccin as an adjunct to local treatment in the resistant follicular forms. Small doses of *x*-rays are very helpful in resistant cases. General hygiene must be watched, and an out of door life recommended to those suffering frequent recurrences.

Pityriasis Capitis.—**Definition.**—Pityriasis capitis is abnormal diffuse scaliness of the scalp, not accompanied by redness. It is divided into P. simplex, common dandruff, a dry scaling which may exist for years and never causes baldness, and P. steatoides, a greasy scaling which often causes gradual loss of hair.

Symptoms.—Pityriasis simplex (dandruff, seborrhea sicca) is the common disease characterized by the production of dry scales, which in severe cases are seen in large numbers on the hair, the collar and shoulders. The scalp under these scales is of normal color, the hair often dry and lusterless. Occasionally a yellow or blood crust is seen, which is ascribed by most authors to scratching, but which I am convinced is the result of a superficial, easily ruptured pustule. The disease is not uncommon in children of six or over, and is very persistent and easily aggravated by neglect of the scalp, errors of diet, disease, especially chronic gastro-intestinal disorders, or any other cause of lowered resistance. It is due, according to Sabouraud, to infection with the bottle bacillus, or spore of Malassez, an organism assuming shapes varying from that of a large thick bacillus to that of a budding yeast cell. It cannot be grown artificially, but is found in small numbers in the normal scalp and in large colonies in the scales of pityriasis. Histologic examination of the scalp shows a hyperkeratosis with the organism superficially in the horny layer. Darier suggests that the hyperkeratosis may be the primary feature, the infection secondary.

Diagnosis.—Pityriasis simplex is the only condition causing diffuse dry scaling without redness of the scalp. Secondary scaling after the infectious fevers, impetigo, etc., is accompanied by redness of the scalp, seborrheic dermatitis and psoriasis by localized red areas covered by scales, pityriasis steatoides by greasiness of the scales. Rarely a diffuse form of ringworm may resemble pityriasis simplex but some loss of hair has always occurred, and the fungus can be found in the hair or scales. Diffuse favus in children whose scalps are often washed may be manifested by scaliness only; but neglect soon results in the reappearance of typical crusts and cups containing the fungus, and the scales are very adherent, leaving erosions when removed.

Treatment.—For ordinary cases, alcoholic lotions are sufficient and much pleasanter to use than ointments. Five-tenths to 2 per cent. salicylic acid in 50 per cent. alcohol, 1 to 3 per cent. formalin in the same menstruum, or the following:

R.	Hydrarg. chlor. corros.	0.1
	Euresol pro cap.	5.0
	Ol. ricini	5.0
	Spts. acidi formici	
	Spts. odorat. aa	25.0
	Aq. dest. ad	120.0

applied once or more a day with friction, give good results. For more severe cases, cold cream containing 1 to 3 per cent. salicylic acid and 3 to 12 per cent. sulphur may be used. This should be rubbed into the scalp once a day. By the second week it can usually be replaced in part by one of the lotions. After the disease is under control, the lotions should be used for months or years to prevent recurrence. Massage, brushing, and the cleaning and sterilization of combs and brushes are necessary here as in all infections of the scalp.

Pityriasis Steatoides.—**Symptoms.**—From the simple form of pityriasis, P. steatoides differs in the greasiness of its scales and the tendency to cause alopecia. It is always preceded by P. simplex, the change taking place slowly, nearly always after puberty. The hair becomes more oily, the scales become larger, yellowish and greasy, the itching increases and the hair slowly becomes thin, as described under seborrhea.

Etiology.—Sabouraud claims that the change is due to infection with his polymorphic coccus in gray colonies, which others consider identical with Unna's morococcus.

Pathology.—The simple hyperkeratosis of P. simplex is replaced by an active inflammatory process consisting of edema with the formation of minute epidermal vesicles, an infiltration of leukocytes about the blood-vessels and in the epidermis, acanthosis, hyperkeratosis and parakeratosis. This histologic picture suggests seborrheic dermatitis, and many authors consider it the mild form of seborrheic dermatitis.

Diagnosis.—Seborrhea, demonstrated by the expression of seborrheic filaments from the follicles, often complicates P. steatoides; but the presence of scales shows that the seborrhea is not alone. Seborrheic dermatitis occurs in sharply defined patches, with redness and sometimes slight elevation of the borders, and the glabrous skin is often involved. Eczema is more acute, with marked itching, inflammation and weeping, and is usually localized. Impetigo is an acute infection, sharply localized, and spreading from one point to another, producing crusts, not scales.

Treatment.—The treatment of P. steatoides is the same as that of the simple form except that it must be more vigorous and more persistent.

Comedo.—**Synonym.**—Blackhead.

Definition.—A comedo is a plug of dried sebaceous material filling the dilated duct of a sebaceous gland or the upper part of a hair follicle. The outer part of this plug becomes yellow, brown or black from pigment originating in the sebaceous substance combined with dirt.

Symptoms.—In children, comedones occur in three forms: The milium-like eruption in infants, grouped comedones in children as described by Crocker, and comedones resulting from applications of oil.

The milium-like eruption of infants is a phenomenon so common that it can hardly be considered an abnormality. At birth and for a few days thereafter the nose, cheeks, forehead and sometimes even the lips and ears are dotted with pinpoint to pinhead sized white macules or round topped papules, thickly set. After pricking the skin, soft sebaceous matter can be expressed. Without treatment they disappear in a few days. Rarely they occur upon the body also.

Grouped comedones occur upon the cheeks, chin, forehead, occiput, chest or back of infants and young children. Local irritation, warmth and moisture are exciting factors. They are closely set, small, firmly situated and rarely cause acne.

The third group, of which several cases have been reported in England, comprises extensive eruptions of comedones upon the chest and back of children who have received repeated applications of camphorated oil. They have been seen to persist and even increase after the use of the oil had ceased, and acne is often associated.

Etiology.—Comedones have been seen as early as the fourth month of development, and are common in the fifth and sixth months. Whether due to the development of the sebaceous glands at the time of the development of the sex glands, which Jaquet and Rondeau have called "puberté en miniature," or whether a response to the influence of the hormones of the mother, as Kraus suggests, they seem always to be associated with a greasy skin.

Pathology.—Kraus, who studied these cases, found that the milium-like eruption cannot be looked upon as a real milium, for in every specimen he found a surface opening, however small in relation to the size of the cyst-like dilation of the duct or follicle. The narrowing of the aperture is due to a hyperkeratosis. The plug itself has often the onion-like construction seen in the comedones of adults, due to the concentric arrangement of flat horny cells.

Treatment.—For persistent comedones, washing with hot water and soap, followed by hot towels and removal of the comedones after loosening their tops, and then the application of an alcoholic solution of resorcin, 3 to 6 per cent. or lotio alba, with or without resorcin, should give prompt results. The prevention of an excess of sweets in the diet, and of oily applications locally, should of course be assured.

Acne Vulgaris Neonatorum.—**Definition.**—A chronic disease of the skin characterized by papules and papulopustules in association with comedones.

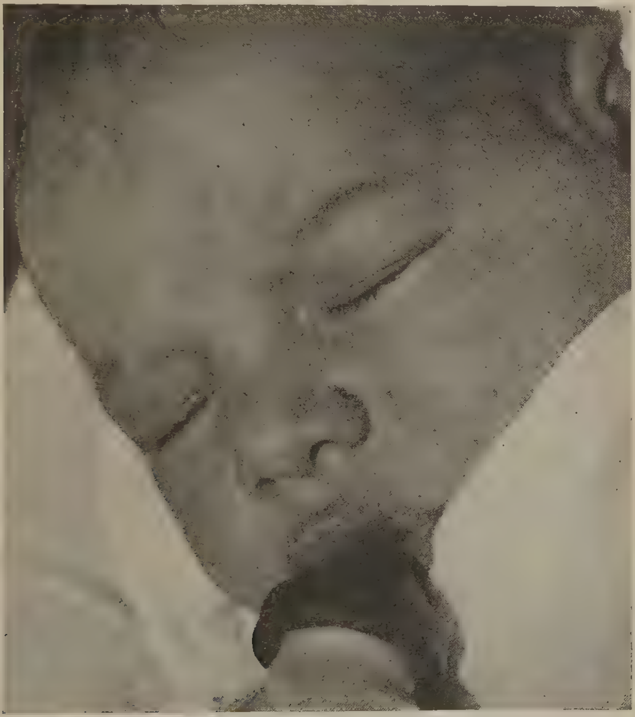

FIG. 73.—Comedones in new born. (Author's collection.)

Symptoms.—Upon the nose, cheeks and the lower part of the center of the forehead are seen bright to dark red papules, often showing at their tips blackheads, sometimes pustules, and between the papules many non-inflamed blackheads. The milium-like comedones were always marked in these rare cases described by Kraus (see reference under comedo) and oilness of the skin of the forehead and cheeks, sometimes with scaliness of the eyebrows, nasal furrows and scalp, was usual. The lesions were all small as compared with those of the acne of adolescence, and scarring was not seen. The acne associated with comedones due to oily applications occurs upon the chest and back as a usual thing.

Etiology.—The inflammation about the follicles is a reaction to the irritation of the comedo, or more likely, to infection with the acne bacillus and staphylococcus added to the mechanical irritation. Irritants in the circulating blood serum have something to do with the formation of pustules, as is evident especially in acne due to the administration of iodids or bromids.

Pathology.—Sebaceous glands are developed far beyond the normal in these cases as studied by Kraus, filling the skin, often far below the level of the lanugo hairs. Cystic dilatations at the mouths of the follicles or at the junction of the sebaceous ducts and follicles are numerous. About the glands, hair follicles and ducts the blood-vessels are dilated, and surrounded by an infiltrate composed of connective tissue cells, lymphocytes and polymorphonuclears. This infiltrate may be absorbed, or may increase, the tissue may break down into a real abscess, and after this has emptied, a new infiltrate of connective tissue cells forms. The latter is always small, never large enough to show macroscopically as a scar.

Prognosis.—All cases reported have cleared spontaneously within a short time.

Treatment.—If any treatment is necessary, that advised for comedo should be sufficient. The possibility of oil applications or iodids or bromids causing the eruption should always be borne in mind.

(C) Diseases of the Hair and Hair Follicles

ATROPHIA PILORUM PROPRIA

Fragilitas Crinium.—**Definition.**—A disease characterized by splitting or brittleness of the hair, usually accompanied by unnatural dryness.

Symptoms.—The symptomatic form, which is by far the most common, is encountered in any disease causing abnormal dryness of the hair as ringworm, seborrheic dermatitis, eczema, psoriasis, general febrile disorders or cachectic conditions, in which splitting of the nails also is often seen.

Usually the splitting occurs at the distal end of the hair, but in the idiopathic cases especially may involve the shaft or even the follicular portion. Duhring, Hyde and Parker have reported cases of intrafollicular splitting. Most commonly, the split hairs are found scattered among normal hair; but sometimes are seen in definite patches.

Etiology.—The causes of the symptomatic cases are easily understood; either direct or indirect interference with nutrition of the hair, and in the idiopathic cases it is assumed that a similar cause is responsible. The dryness is to be considered more as an accompanying than an etiologic factor.

Pathology.—Some uneveness of the hair shaft is usually seen, and rarely an atrophy of the bulb is present. Spiegler claims that a motile, spore forming bacillus, discovered by him, is responsible for the disorder and that inoculation of healthy hair with this organism has caused the disease. This has not been confirmed by others.

Treatment.—General treatment tending to increase the nutrition of the skin and local use of oily stimulating lotions such as the bichlorid euresol lotion recommended for pityriasis capitis, applied once daily, are to be recommended. Massage, so valuable in scalp stimulation, is avoided here for fear of injuring the delicate hair and increasing the splitting. Clipping, or even shaving is advised for severe cases.

Monilithrix.—**Synonyms.**—Moniliform hair. Beaded hair.

Definition.—A malformation of the hair consisting of constrictions at fairly regular intervals, giving a beaded appearance. It is usually congenital and associated with keratosis pilaris.

Symptoms.—The constrictions are long, making the sections between them, which are of normal thickness, fusiform in shape. In dark haired persons the constrictions are lighter in color than the nodules, while in blondes the reverse is the case. The nodes are of the normal thickness and color and retain the medulla, which is absent from the internodes. The hair breaks easily at the thinned places. The deformity is present throughout the length of the hair, even within the follicle, where the inner root sheath was found by Guzman to be homogeneous, allowing no differentiation of the layers. The outer root sheath was thickened opposite the constrictions. The disease is usually localized, oftenest on the occiput, but it may involve the whole scalp, and sometimes the eyebrows and the hair of other parts of the body. At birth or soon after the hair is seen to be short and crinkly, not over ¼ in. long, sometimes so short as to appear only as black spots at the tips of the hyperkeratotic follicles. Improvement is sometimes seen, but cure seldom.

Etiology.—The disease is nearly always hereditary, and tends to descend in the same sex throughout the family. It is classed among the congenital malformations, along with keratosis pilaris, with which it is almost constantly associated.

Treatment.—The treatment is the same as that of keratosis pilaris, salicylic ointments or oily lotions. Olive oil 75 per cent. and glycerin 25 per cent. is a good menstruum.

Trichorrhexis Nodosa.—**Synonyms.**—Trichoptilosis. Nodositas crinium. Trichoclasia. Clastothrix.

Definition.—A disease characterized by the formation of swellings at intervals along the hair shaft, and easy fracture at these places.

Symptoms.—The disease occurs usually in adults but may occur in children with long hair. It appears as from one to five grayish-white swellings along the hair shaft, usually in its upper third. At these places the fibrils are often separated, so that the node resembles two brushes pushed together until their fibers interlock. Many hairs are broken off, presenting brush-like, frayed ends, and if close together a singed appearance may result. In red hair the nodes may be black instead of gray.

Etiology.—Three theories have been presented:

1. That it is a result of dryness or atrophy of the medulla resulting from lack of nutrition.

2. That it is due to mechanical causes, rough handling, or nervous twisting of the hair.

3. That it is due to an infection with a multiform bacillus, described first by Hodora, later by Spiegler, Markusfeld, von Essen and De Keyser. C. Beck believes that it may be due to any one of various organisms. The first mentioned cause is probably the most important, as Heidingsfeld concluded after a careful study of the disease. He states that the condition "is universally present in long, uncut hair as a normal condition" and is only abnormal when the nodes are present at other points than the distal ends.

Pathology.—The hair swells at some point and forms a node, a transverse fracture appears through the node, the neighboring shaft, from which the medulla has disappeared, splits into many fine fibrils, and the fracture becomes complete.

Diagnosis.—The gray swellings may be taken for nits until closely examined, when their true nature is easly determined. From monilithrix it is distinguished by the familial occurrence of the latter, the shortness of the hair, the accompanying keratosis pilaris, and the fact that in monilithrix the fracture is through the constricted part, in trichorrhexis always through the node.

Prognosis.—The disease is very resistant to treatment; but recovery sometimes results after long continued effort.

Treatment.—Two distinct and opposing lines of treatment are advocated. Those who believe that the trouble is caused by lack of nutrition use vigorous stimulation, strong lotions or ointments of sulphur, pyrogallic acid, or tincture of cantharidies applied with massage. Others, who claim that mechanical injury is the cause of the disease, find no difficulty in explaining the failure of such treatment. They advise very careful handling of the hair and the gentle application of oily lotions. The few cures recorded have been the result of long-continued treatment and the successful element in the treatment is somewhat in doubt. Stimulation with oily preparations and gentle massage combine the good elements of both methods.

Canities.—**Synonyms.**—Grayness. Leukotrichia. Poliosis.

The occurrence of gray or white hair in childhood is a rarity. It may be congenital or acquired. Congenital cases are classed as albinism, complete or partial. The latter are sometimes seen occurring in succeeding generations in patches involving exactly the same area, usually near the front of the scalp, in every case. The hair is usually white and the patch sharply defined, but may shade off gradually into the normal color. Hereditary cases in which the white hair appears later in childhood belong in the same class. In total albinism, pink eyes and deafness are associated.

Acquired grayness occurs occasionally in childhood as a sequel of the infectious diseases, or in connection with nervous diseases, as epilepsy, brain tumor, or injury to nerve trunks. I have recently seen a case of diffuse partial grayness of the new growth of hair after total epilation with *x*-rays for favus. The sudden blanching of the hair from shock has been noted in childhood. Local disease of the scalp, as leukoderma, may cause patches of gray hair. Alopecia areata sometimes causes a growth of white hair, later replaced by hair of normal color, but the first growth in this disease is usually light blonde rather than white.

The hair of canities is usually white throughout its length, but sometimes only in the proximal or distal part. Gray hair is due to an admixture of white hairs among those of normal color. The blanching is due to loss of pigment, aided in some cases, especially in sudden blanching, by the production in the hair, or the introduction into it, of some gas which by its light reflex conceals the pigment.

Rarely the hair turned suddenly gray is slowly restored to its normal color, and this sometimes occurs also to the gray patches of leukoderma, while it is the rule in alopecia areata. Otherwise there is no hope of a restoration of color except by dyeing, which is seldom justifiable. If done, care must be observed, for many of the proprietary hair dyes cause severe dermatitis at times.

Ringed Hair.—This is a rare variation of canities in which alternate lengths of the hair shaft are blanched, without any change in the diameter of the shaft. Landois showed that the light colored parts contained more air in the medulla than the parts of normal color. No satisfactory explanation of the cause of the phenomenon has yet been offered. It is easily differentiated from trichorrhexis nodosa, with which it is sometimes associated, by the normal contour of the hair shaft. The same fact differentiates it from moniliform hair. Cases in which the condition was apparently secondary to neuralgia have been cured by relief of the neuralgia. Usually treatment is as unavailing as in ordinary canities. A large proportion of the few cases reported have occurred in children.

Alopecia.—**Synonyms.**—Calvities. Acomia. Baldness.

Aside from that due to alopecia areata, considered under a special heading, alopecia is rare in children. It may be congenital or acquired. Congenital alopecia is usually partial and often associated with defective development of nails and teeth and sometimes with syndactilism, defects of sweat and sebaceous glands, atrophy of the skin of the finger tips, epidermolysis bullosa, or xeroderma. The partial alopecia of monilithrix has already been mentioned. Much less often than that disease, is ordinary congenital alopecia inherited. It affects boys much oftener than girls. According to Hyde the hair may be completely absent at birth and never grow, the infant may be born with scanty lanugo hair, or this may replace normal hair which was present at birth. Most cases show some rudimentary hair, though there are cases on record in which there was complete absence of hair follicles.

Alopecia Symptomatica.—Acquired alopecia in children is symptomatic and may be of general or local origin. That resulting from general conditions usually takes the form of defluvium capillorum, in which, from one to six months after an acute fever the hair suddenly begins to fall out. This seldom goes on to complete baldness. When due to acute conditions the hair returns in a few months; but in the cachexia of tuberculosis, mycosis fungoides, or diabetes mellitus, or in myxedema, the restoration of the hair is less certain, depending on the degree to which normal circulation can be restored to the follicles. A temporary toxic alopecia has occurred from the internal administration of thallium acetate or boric acid. The alopecia sometimes seen after the abuse of mercury belongs among the cachectic group. Defluvium capillorum often occurs in exfoliative dermatitis, whether idiopathic or due to drugs, as antipyrin, mercury or arsphenamin. Acquired syphilis in the early secondary stage causes a patchy alopecia in about 10 per cent. of the cases. The patches are small and not sharply defined, giving the hair a ragged appearance well described as moth-eaten. Rarely it imitates alopecia areata by causing sharply defined, larger patches. Unlike alopecia areata, the patches are all small, about the same size and approximately symmetrical. Other signs of syphilis, the serum test, and the prompt restoration of the hair upon anti-syphilitic treatment make the diagnosis clear. This typical patchy, moth-eaten alopecia does not occur in congenital syphilis. Most authorities mention alopecia as a symptom of the congenital form of the disease; but fail to agree upon any definite appearance. Neumann says that the hair of the scalp, brows and lashes is thin and absent in places. Marshall mentions thinning of hair, eyebrows and lashes as of frequent occurrence and says that bands of alopecia may be seen on the sides and back of the scalp. Hutchinson speaks of a rapid growth of very dark hair which he calls the "syphilitic mop."

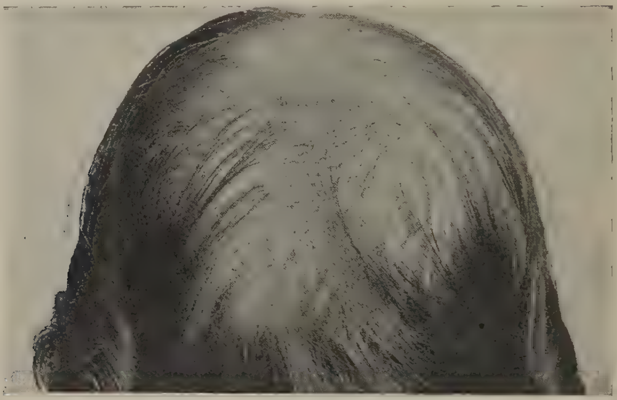

Fig. 74.—Roentgen-ray alopecia following the making of roentgenograms of the sinuses. (Ormsby and Mitchell.)

Still says that he has seen this "mop" in 4 per cent. of his cases, and a marked alopecia, especially at the vertex, in 6 per cent. Evidently the alopecia of congenital syphilis is an indefinite one of no diagnostic value. Temporary baldness in patches sometimes follows impetigo or erysipelas of the scalp and forms part of the clinical picture of ringworm of the scalp. Roentgen alopecia may be universal or in patches, either sharply defined or not, depending on whether the exposure was limited by a shield applied closely to the head. It appears suddenly one to three weeks after a single exposure or may occur during a series of exposures and may be accompanied by other signs of Roentgen dermatitis, such as redness, itching or burning sensations. Because removal of the hair requires less than an erythema dose of the rays, it may occur without the least redness. Unless a marked reaction has occurred, the prognosis for full restoration of the hair is excellent, though months may elapse before the growth appears.

Permanent baldness in patches follows any scarring disease, as ecthyma, tertiary or sometimes secondary syphilis, confluent small-pox, favus, lupus erythematosus, folliculitis decalvans or morphea. Trichotillomania, a rare nervous disease in which the patient has the habit of pulling out the hair from some small area on the scalp or eyebrows, causes a temporary alopecia in patches. Sutton reports a case in a boy of 14.

Treatment.—Defluvium capillorum is probably little affected by treatment, the hair growing again to its former condition without treatment in practically all cases. It is best, however, to give the parents the satisfaction of making local applications, such as alcoholic lotions of resorcin or euresol, 3 to 6 per cent., or of salicylic acid, 1 to 3 per cent. The idea that shaving the scalp produces a better growth should be discouraged. Syphilitic alopecia needs no treatment except that of the general infection, though lotions containing bichlorid of mercury in alcohol up to 1 per cent. may have some specific effect as well as a stimulating action. If papules are present, the frequent application of the ointment of ammoniated mercury will hasten their disappearance. The cachectic alopecias depend for improvement upon the treatment of the causative conditions; but local stimulation should not be neglected. In Roentgen alopecia care should be taken to avoid any irritation. Petrolatum or cold cream containing 12 per cent. boric acid is a good soothing application. Congenital alopecia is hardly amenable to treatment, though a salicylic ointment or oil and glycerin lotion for the associated keratosis pilaris might be of some use.

Alopecia Areata.—**Synonyms.**—Area Celsi. Alopecia circumscripta.

Definition.—A disease characterized by sudden, complete loss of hair in sharply defined areas, usually without signs of inflammation.

Symptoms.—Wholly without warning, a bald spot is discovered by the mother or nurse. The skin of this area, usually one to several centimeters in diameter, may be slightly reddened and swollen; but is oftener neither elevated nor depressed, of normal color and perfectly smooth. The patch is sharply defined by apparently normal hair. Near the borders, during the progressive stage, loose hairs can be found, often broken off and atrophied in the follicular portion, taking the shape of a club or an exclamation point. From day to day this patch can be seen to spread peripherally, either in its whole circumference or only on one side, and careful search reveals other similar patches occurring here or there, apparently by chance. With or without treatment, the extension may stop with one or a few small patches, or may rapidly go on to involvement of the whole scalp, or even the whole body. The patches usually remain discrete, but in the more severe cases merge to form large ones. Usually no symmetry is observed, but in some cases the eruption is fairly symmetrical. Sometimes the initial patch occurs just within the hair-line of the occiput, and extends along the border of the scalp even to the temples and forehead. Because of the serpentine shape or progression of these patches these cases were named ophiasis by Celsus. Severe cases of alopecia areata result in marked disfigurement with the most bizarre arrangement of the bald areas or total baldness, rarely involving even the whole body.

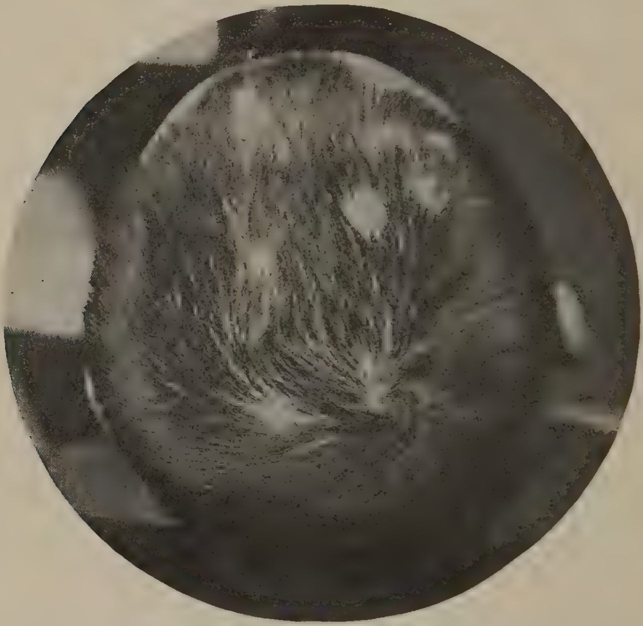

FIG. 75.—Alopecia areata. (Collection of Dr. W. A. Pusey.)

Etiology.—The disease rarely occurs under five years of age; but is common between 5 and 15. Both sexes are equally liable. Three theories of its causation are to be considered:

1. The dystrophic theory.
2. Direct nerve influence.
3. Infection.

The first of these, supported by Jacquet, attempts to explain the disease as the result of reflex nerve disturbance from various sources, ranging from dyspepsia to tuberculosis and vesical calculus. Most of the cases are held to be due to carious teeth. Few other authorities are able to substantiate these claims. In respect to the second theory, alopecia areata has so often followed immediately after shock, operative or accidental injury to nerves or after nerve disease that it must be granted that there are cases dependent in some way upon this cause. The infection theory is supported by the occurrence of epidemics in schools and barracks, and among those using the same bedding. The mode of onset and the course of the disease are in favor of this theory in spite of the negative results of the search for parasites in the hair and skin by direct examination, culture and inoculation experiments.

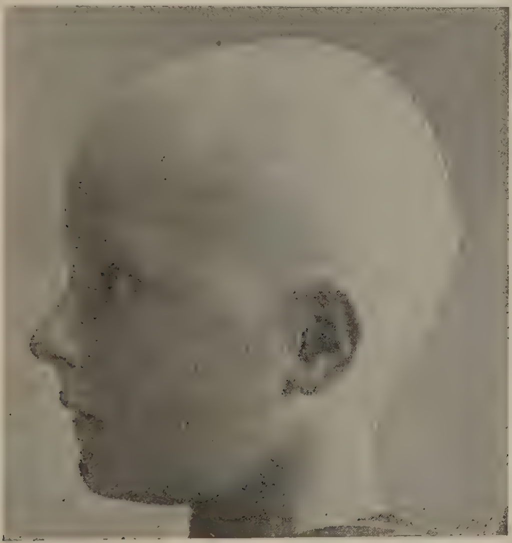

Fig. 76.—Alopecia areata universalis. (Collection of Dr. Grover W. Wende.)

Pathology.—Dilatation of the blood and lymph vessels in the upper corium and about the hair follicles is seen, and an infiltrate described by various authors as composed of leukocytes, connective tissue cells, or lymphocytes and mast cells. The changes in the hairs are like those of senile alopecia, according to Duhring, except that they appear more abruptly. Narrowing of the shaft just above the lower end produces the exclamation point appearance of Crocker. Disappearance of the medulla, loosening of the cortical cells, increase of air between them and changes of pigment have all been noted.

Diagnosis.—From ringworm, alopecia areata is distinguished by its rapid onset and spread, its smooth skinned, wholly bald areas, its absence of fungi, scales, vesicles and crusts, and of inflammatory patches on the glabrous skin. From the rare cases of "bald ringworm" the absence of the fungus and perhaps the more rapid spread are the only distinctive points.

From syphilitic alopecia it is differentiated by the course, usually one or a few patches being succeeded by others while the older ones increase in size. In syphilis, a large portion of the scalp takes on very rapidly the typical ragged appearance, always symmetrical, not displaying the distinct, completely bald spots of alopecia areata. Rarely syphilis produces a good imitation of alopecia areata in small patches; but these are all nearly of the same size, occurring simultaneously, instead of one or a few large patches followed by several smaller ones, as in alopecia areata.

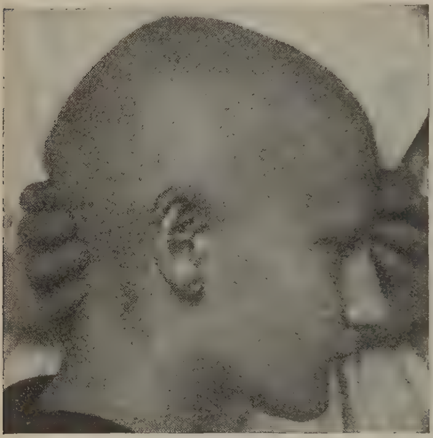

Fig. 77.—Alopecia totalis. (Author's collection.)

Impetigo, erysipelas, or other violent inflammations of the scalp can cause temporary bald areas; but there is always a history or signs, such as redness, of the preceding disease. Lupus erythematosus, favus, etc., can be differentiated by the scars and other evidence of these diseases.

Prognosis.—This should be guarded, keeping in mind the inherent captiousness of the disease. Especially guarded must be the prognosis in severe cases; but the patient should always be encouraged to hope for a cure, though it may be long delayed. Under successful treatment a growth of fine hair soon appears on the patches, very light blonde, sometimes white, gradually growing darker as it lengthens. This may fall out, to be replaced by a similar growth and this may in turn fall; but eventually a permanent growth is established. Even the malignant form causing total alopecia is likely to get well if downy hair appears within a few months. The non-progressive form following nerve lesions practically always recovers; but there is more liability in these cases of the hair remaining white.

Complications.—The disease is rarely associated with vitiligo. Scleroderma and dystrophies of the nails have been described by a few writers in association with it.

Treatment.—The general health of the patient must be restored if below par. Focal infections should be found and eradicated. Arsenic is recommended, especially for cases in which a nervous etiology is suspected. Pilocarpin hypodermically has been recommended; but the results are so seldom satisfactory that it should be tried only in severe cases refractory to less dangerous remedies. In most cases no special indication for general measures can be found. Locallv, the indication is sharp irritation of the bald areas to promote the prompt growth of hair, and strong lotions for use over the whole scalp to check, if possible, the spread of the disease. The lotion may contain bichlorid up to 0.5 per cent. strength, resorcin up to 6 per cent., formalin 1 or 2 per cent., or any one of a dozen other antiseptics. The menstrum should be alcohol, to provide for penetration and rapid drying. Oil may be added to the lotion or used afterward. The bald spots should be painted with phenol or cresolic acid, 50 per cent. or stronger, enough to produce a sharp reaction followed by exfoliation. On the glabrous skin, weaker solutions must be used. The application should not be repeated until the reaction and exfoliation are completed. Formalin in strong solution is highly recommended, but is quite painful to some people. Chrysarobin in a 2 to 10 per cent. ointment, or in chloroform as a paint, is effectual; but the greatest care must be used to protect the eyes, for it is not easy to avoid conjunctivitis when this drug is used on the scalp. A varnish of flexible collodion applied over the chrysarobin may prevent the spread of the drug. Faradic or high frequency electricity is useful in some cases, and *x*-rays in less than half the erythema dose have given good results. The ultra-violet light of the Alpine sun or Kromayer quartz lamp is probably the most constantly effectual of all local measures. Strong applications producing a rather violent reaction seem to be most quickly beneficial; but great overdosage should be avoided, as it sometimes results in a deep edema, lasting, in one case in my experience, two weeks, the swelling slowly descending from the scalp over the face.

(D) DISEASES OF THE NAILS

The nails are affected by developmental defects, changes in nutrition due to general disease, or by local injury or disease. Changes in the nail plate may be acompanied or preceded by visible alterations in matrix, nail bed, or nail folds, or may occur alone. Few of the nail conditions are pathognomonic of any particular disease. Disturbances of nutrition often show early and marked effects upon the nails, due possibly, as Pusey suggests, to the fact that they are at the end of the circulatory loop. Study of the histologic pathology has been hampered by the great difficulty of obtaining biopsies on this portion of the body.

Atrophia Unguium.—**Anonychia.**—Absence of nails may be congenital or acquired. An example of the former kind has been reported recently by Charteris, in which finger and toe nails were absent from the three inner digits, the fourth had a half nail, while the nails of the little fingers and toes were normal. These malformations are often associated with defects of the hair and teeth.

Local injuries, burns, freezing, or infection are the common causes of loss of nails. Rarely it results from exposure to x-rays, scleroderma, epidermolysis bullosa, gangrene, syphilis or leprosy. Permanent loss of nail forming tissue, with scar formation, is responsible in many of these cases for the nail defects, which vary from total absence of nails to all degrees and forms of horny rudiments.

Onychomadesis.—Shedding of the nails usually affects the big toe, but may occur on all fingers and toes. It is part of the rare condition known as keratolysis, in which an annual shedding of the skin takes place. It may occur, as in the familial cases reported by Montgomery, as an hereditary peculiarity without other abnormality. It is sometimes an early symptom of tabes, and occurs after nervous shock, in diabetes, syphilis and alopecia areata. Secondary to changes in the soft tissues it occurs in acute scaling processes, as psoriasis or exfoliative dermatitis, following the acute infectious fevers, and in syphilis.

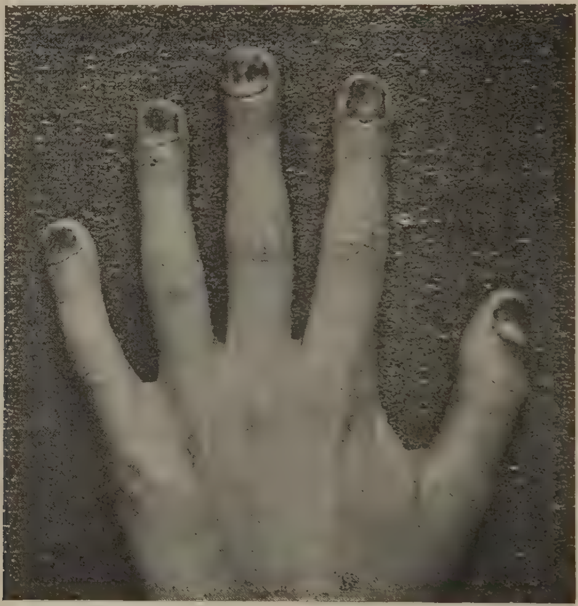

Fig. 78.—Atrophy of finger-nails associated with alopecia areata in a girl of 12 years. (Collection of Dr. Grover W. Wende.)

Onychoschizia.—Partial loosening of the nails may be caused by these same diseases, or by a number of other conditions, as pityriasis rubra pilaris, eczema, the ringworm infections, or tumors under the nails. It occurs as a result of mechanical or chemical injury, neuroses often associated with hyperidrosis, or idiopathically, especially in children, in whom slight loosening of the nails at the border is not uncommon.

The loosened portion may become again adherent and normal, or it may extend to total loss of the nail.

Thinning of the nails may be congenital, with the usual associated involvement of hair and teeth, or may result from any of the causes already cited for loss of nails. The abnormally thin nails may appear as:

Koilonychia (spoon nails) in which the normal convexity is changed to concavity with raised and sometimes loosened edges, or as:

Eggshell nails, described by Hyde, in which the loosened edges of the thin nail plate showed purplish-white, like the inner surface of an eggshell.

Grooved nails, usually transversely grooved, are the commonest form of the disorder, occurring in many skin diseases and in general diseases, and often give accurate evidence of previous attack or attacks of disease. Thus in typhoid with relapses, a groove may represent each attack. Even such apparently localized disorders as epididymitis, or disturbances like sea-sickness or child-birth may cause them. Hereditary familial furrowing of the nails is recorded by Török as "*hypoplasia ungius intermittens hereditaria.*" Many times no cause can be determined. Longitudinal furrows occur less often from the same causes as the transverse form. Brittleness of the nails occurs with especial frequency with this form.

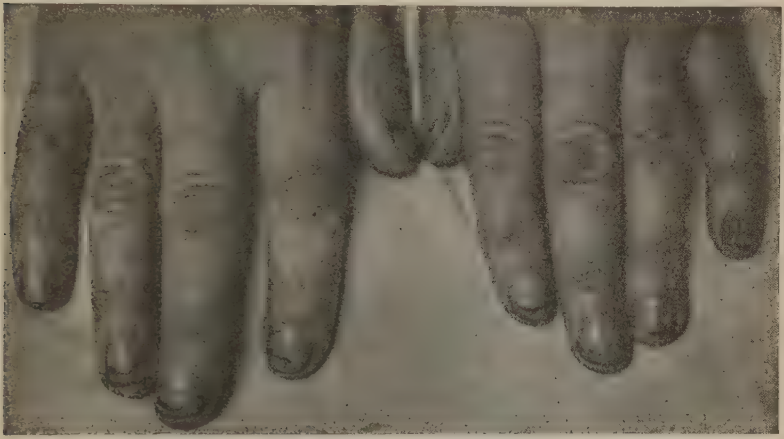

FIG. 79.—Grooved nails in dermatitis herpetiformis. (Author's collection.)

Splitting.—This is seen not seldom in syphilis, less often in other causes of malnutrition of the nails. In some cases whole sheets of nail plate separate.

Leukonychia.—White spots, white stripes, or total whiteness of the nails appear as a result of local injury from too vigorous retraction of the nail fold, or in handworkers, or from general causes as typhoid, alcoholic neuritis, or syphilis, or many less serious disturbances of health. Familial cases are recorded. It has always been explained as due to air between the layers of the nail plate, but Heidingsfeld and other writers have found parakeratosis in these areas, to which they ascribe the white appearance.

Treatment.—In these atrophic conditions, when acquired, treatment may be directed to the causative disease and to improving nutrition. It is often without result. Arsenic internally, and mercurial plaster, or tar preparations locally, perhaps also *x*-rays, may be tried. Of course when due to general diseases, as syphilis, improvement may be expected as the result of general and local treatment of the causative disease.

Onychauxis.—Thickening of the nails is seen as a part of keratosis palmaris et plantaris, pityriasis rubra pilaris, ringworm, favus, etc. It may be due to local injury, as pressure of tight shoes or in connection with hammertoes, or it may be congenital in the same class of cases as atrophy of the nails, and often in association with it. The deformed nails are more convex, transversely and sometimes longitudinally, than normal, and are opaque yellow, brown or black. Owing to the difficulty and pain of trimming them, they often project more or less beyond the end of the digit, and becoming curved, cause the grotesque deformity known as *onychogryphosis* (griffin nails). Great strength, twisting curves and blackening sometimes cause these nails to resemble miniature ram's horns. Another form of onychauxis, Hippocratic nails, is associated with clubbed fingers, usually in chronic diseases of the heart or lungs.

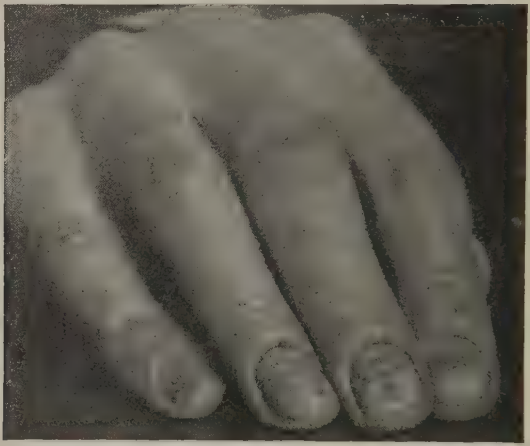

Fig. 80.—Grooved nails and paronychia due to chronic eczema. (Author's collection.)

Imperfect formation of horny tissue in these cases causes brittleness of the nails, and the accumulation under the free border of soft, partly cornified tissue. Thickened nails occur more often on the toes, especially the big toe, than on the other digits.

Ridged nails is a form of partial onychauxis in which parallel ridges, usually longitudinal, are present. Sometimes the thickening is at the center only, causing an angular elevation like a gable roof.

Treatment.—The cause of the thickening determines the treatment. When the cause is unknown or cannot be corrected, softening the nail with salicylic ointment or plaster, followed by paring or grinding the nail into proper shape, will usually give satisfaction but must be repeated as required. Careful use of x-rays gives good result in many cases of abnormal nail growth unaffected by other treatment.

Pterygium.—The posterior nail fold, becoming adherent to the nail plate, is carried out with the latter as it grows, and forms a wing-like extension over the lunula. This abnormality may be congenital, or due to x-ray exposures, but is usually the result of poor hygiene. The treatment is mechanical, pushing back the fold of skin or cutting it.

Ficus Unguium.—Rarely the posterior nail fold retracts, exposing the root of the nail. This is the result of disease or injury of the matrix. Treatment must be directed to the underlying cause, if that can be found, or to local stimulation by drugs or electrical or actinic agents.

Onychia and Paronychia.—These result often from ordinary pus infection, gaining entrance commonly through hang nails, or they may be due to trauma (for instance the pressure of ingrowing toe nails) or to chronic diseases, either local, as ringworm, eczema, etc., or general, as syphilis or psoriasis.

Acute Paronychia.—Acute infections of the nail wall are common, due in nearly all cases to entrance of pus organisms by means of a hang nail. They are of importance because of the great pain from swelling of so tense and sensitive a tissue as that of the terminal phalanx, and because of the easy ascent of infection along the tendon sheaths. The treatment is surgical, early opening and drainage of the pus pockets, followed by wet dressings of saturated boric solution containing a small percentage of alcohol, or of Dakin's solution of sodium hypochlorite. Warning against the use of any but the very weak solutions of phenol in wet dressings is necessary, as gangrene of the finger has occurred as a consequence of wet dressings of 1.5 per cent. phenol.

Unguis Incarnatus.—Ingrowing nail is the most common painful disorder of the nails. It is caused by narrow-toed shoes. The edge of the big toe nail grows under the nail fold, which becomes inflamed and swells, adding to the pressure. The remedies are prevention, by wearing shoes with wide toes, elevating the corners of the nail with a tiny cotton packing, drawing down the nail fold with adhesive plaster, or, finally, excising a wedge-shaped piece from the nail fold, thus drawing it away from the nail.

Eczema of the nail bed and walls causes various forms of atrophy or hypertrophy of the nail plate, opacity, furrowing, pitting, splitting, and breaking, thinning or thickening. The first change is seen usually at the root of the nail. Occupational dermatitis causes the same changes as eczema, and is by far the most common cause. The remedies indicated for the same sort of eczema elsewhere are to be applied to the nails with even more patience than is required for eczema of other parts. Soothing oils or ointments, as boric acid 4.0 in rose ointment 30.0 for the acute cases, and graduated stimulation by crude coal tar, oil of cade, oil of beech-wood tar, resorcin, salicylic acid, sulphur, etc., for the chronic forms, are to be used. Arsenic internally, or the cautious use of *x*-rays locally, may be of great assistance in the chronic forms.

Psoriasis.—Occurring with psoriasis of other parts, it commonly appears as a loosening of the side of the nail plate near the free border, and a coincident opacity of the plate, with a granular mass under it.

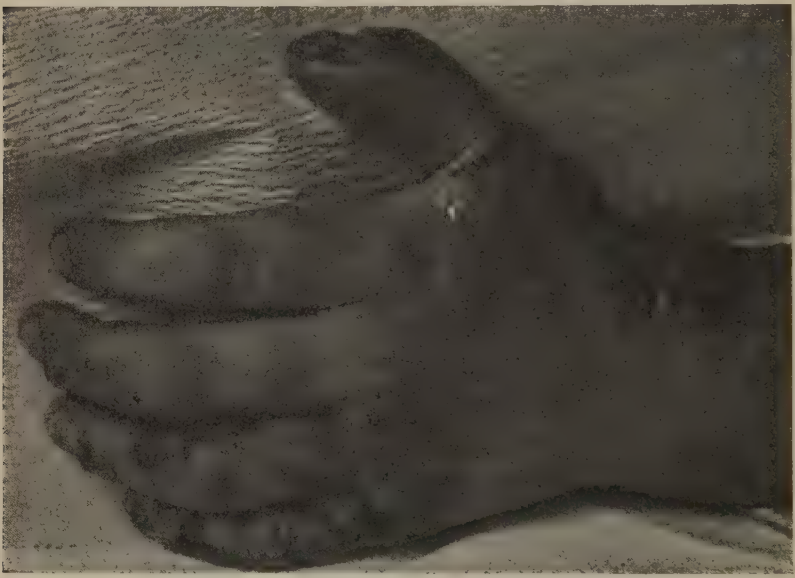

Fig. 81.—Eczema of thumb nail. (Author's collection.)

The affected portion is friable and is often cut away by the patient before examination. A patch of psoriasis on the neighboring nail wall can sometimes be seen. The lesion progresses along the side of the nail towards the root, differing in this respect from eczema, which usually begins at the nail fold and spreads forward. Pitted nails are also common in this disease, causing an appearance like that of the surface of a thimble. More marked changes cause transverse furrows or a general breaking up of the nail plate. Partial loosening, from formation of horny tissue under the plate, is sometimes seen. The treatment of psoriasis of the nails is slow and difficult. The attempt to control the disease by diet low in proteids may be made in suitable cases, though in my experience it seldom succeeds. Arsenic, while well borne by children, and often successful in clearing up the eruption, must not be used in acute cases, which it sometimes aggravates, nor should its use be continued for long after the eruption disappears, for fear of the production of pigmentation and keratoses. The palms and soles should be watched during its administration. Salicin, the alkalies, especially sodium acetate and citrate, may be tried. Locally, if discoloration is to be avoided, 10 to 20 per cent. sulphur or 5 to 10 per cent. beta naphthol may be tried. Chrysarobin, 2 to 10 per cent. in ointment, or 20 per cent. in flexible collodion, is more active. *X*-rays, used cautiously, may be resorted to when other methods fail.

Syphilis of the nails may occur in any stage of the disease. Chancre occurs sometimes in the nail fold by infection by means of a hang-nail, and these cases often have a coincident sepsis masking the luetic infection. Even if no such complication is present, the application of various antiseptics has usually altered the appearance of the sore, and made the discovery of spirochetes difficult or impossible. During the secondary stage the disease commonly causes a paronychia, usually affecting several fingers and usually fairly symmetrical. The nail becomes thickened, dark red and scaly, and extension to the nail bed gradually takes place. Or the lesion may be an onychia from the beginning, showing as a papule under the nail, with the gradual formation of furrows, opacity, blackening, splitting, thickening, or other deformity, or sometimes loss of the whole nail. Malignant cases occur, in which ulcerations occur in the nail wall or bed, the nails turn black and are soon shed, and the whole phalanx swells and is painful. This involvement of the terminal phalanx is seen most often in congenital syphilis, though here also mild onychia sometimes occurs, with opacity, thickening, furrowing and friability of the nails.

Tertiary syphilis affects only one or a few digits, and is usually unilateral. It is less common than the secondary form. The syphilitic nail lesions are usually slow in onset and very slow to respond to treatment, with a marked tendency to recur. Energetic general treatment is needed, sometimes with removal of the degenerated nail by scraping or filing, and the application of white precipitate ointment or a wet dressing of weak bichlorid solution.

Onychomycosis.—Synonym.—Ringworm of the nails.

Symptoms.—Both the tricophytons and the achorion of Schoenlein are responsible for nail infections in rare instances, especially rare in children. Usually associated with involvement of the scalp or the glabrous skin, the nail infection is sometimes the only manifestation of the disease. Beginning at the free border or at the sides, the nails become opaque grayish or yellowish, thickened, furrowed, ridged, and brittle. Favus of the nail sometimes begins as a distinct yellow macule under the nail plate. In old cases the nail may be partly destroyed, only deformed fragments remaining. The microscopic demonstration of the fungus in filings or scraping of the nail is more difficult than in infections of the hair or skin. Of course more time should be given for softening the fragments in the hydroxid solution. Cultures also are more diffiult to obtain. Such demonstration of the fungus is necessary to the diagnosis in the cases in which the nails are the only part affected. Usually only one or a few nails are involved, while other causes of onychauxis affect many fingers and toes, often in a symmetrical manner.

Treatment.—The treatment of ringworm of the nails is very difficult, depending upon removal of the nail by means of caustic potash or soda solutions, and the application of wet dressings of 15 to 25 per cent. solution of sodium hyposulphite, or white precipitate or calomel ointment. Iodin solutions, as Gram's solution, are also valuable, but the staining is sometimes resented. These applications are to be worn under a finger cot, with care to avoid constriction of the finger. Harrison's method, scraping the nail and then applying on cotton 1 part iodid of patassium to 4 each of liquor potassæ and water, for 15 minutes, then a dressing of 1 per cent. bichlorid of mercury in

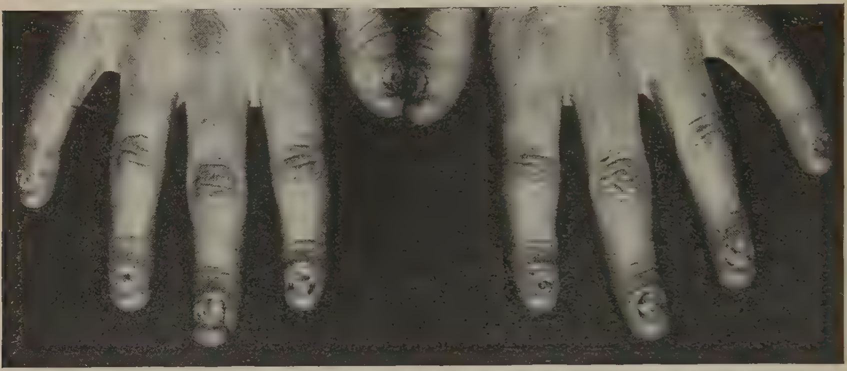

Fig. 82.—Onychomycosis. Ringworm of nails. (Collection of Dr. Grover W. Wende.)

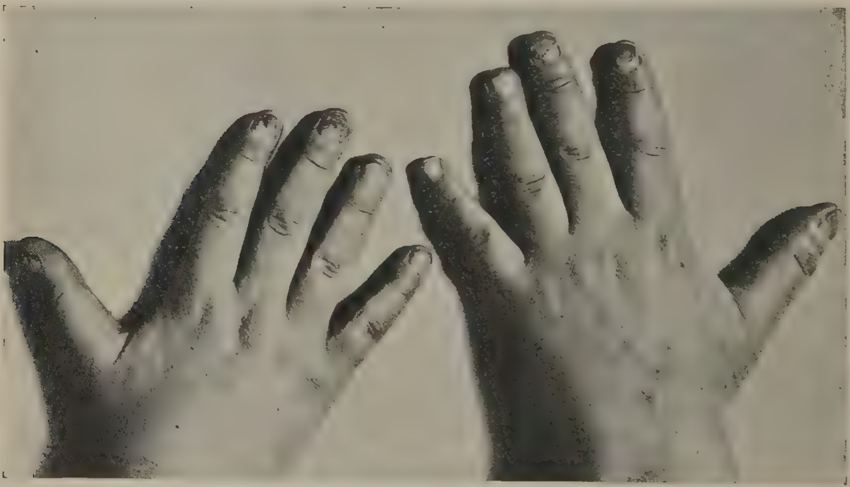

Fig. 83.—Ringworm, nails, boy. (Fordyce and MacKee.)

50 alcohol for 24 hours, has been very helpful in some of my cases. Long-continued treatment is necessary to a cure. Unlike ringworm of the scalp, the nail involvement does not tend to be self limited. Cases are recorded in which the nails were affected for from 20 to 50 years.

(E) DISEASES OF THE MUCOUS MEMBRANES

Owing to the fact that several of the diseases of the skin are accompanied by mucous membrane lesions, it is necessary to describe also those diseases of this tissue that do not form part of any skin disease, but often come under the care of the dermatologist.

Transitory Benign Plaques of the Tongue.—Synonyms.—Wandering rash. Geographical tongue. Exfoliatio areata linguæ. Glossitis areata exfoliativa. Erythema migrans circinate. Eruption of the tongue. Annulus migrans. Ringworm-like patches on the tongue. Pityriasis linguæ.

Symptoms.—This peculiar disease, occurring most frequently in children, begins with the formation of a pinhead-sized, grayish or yellowish, slightly elevated spot on the dorsum of the tongue, usually near its tip. It sometimes is mistaken for a vesicle. The spot enlarges rapidly and clears at the center, leaving a slightly depressed, smooth or scaly, red surface, while the borders retain the original dull gray or yellowish appearance. The circle thus formed may be broken on reaching the border of the tongue, continuing to spread on the dorsum only, or less commonly, the other segment spreads over the under surface of the organ. In from 1 to 10 days, after reaching an average diameter of from ½ to 1 in., the circle fades or, as described by Butlin, grows smaller until it disappears. Soon afterward or during the course of the first, other lesions appear and follow the same course. At times the disease remits, leaving the tongue entirely smooth for a while, then recurs. Sometimes a second lesion appears within the first, forming two and even three concentric rings. When two lesions meet, one of them loses its border, allowing the other to advance (Butlin). Rarely they appear on the under side of the tongue. Usually the lesions are sharply defined and circular or oval. The color of the borders varies from grayish white to dull or even bright golden-yellow, sometimes bluish or silvery white. The disease is chronic, new lesions appearing, running their course in a few days and disappearing to be followed promptly by others. This wave-like succession goes on for years, tending to die out as the patient grows older. Usually no subjective symptoms are present, though some patients have complained of itching. Parents are often greatly concerned, fearing that the lesions are syphilitic.

Etiology.—The disease is rare, occurring more in children than in adults, most of the cases in children under six. It has nothing to do with syphilis, but is probably due to some gastro-intestinal disturbance occurring often in debilitated children. A case of mine in an adult who acquired syphilis during the course of the transitory plaques, regularly grew worse during mercury treatment and improved in the intervals of treatment. Besnier thought it part of seborrheic eczema; Barker, Hutchinson and Kinnier associated it with ringworm; but no support for these theories has appeared. It has been familial in several instances.

Pathology.—The pathology, according to Parrot, consists of an infiltration of lymphocytes about the vessels, with parakeratosis and swelling of the horny cells and proliferation of the cells of the Malpighian layer. Unna thought it a disease of the superficial epithelium.

Diagnosis.—No other disease produces the sharply defined gyrate lesions of rapid evolution characteristic of this one.

Prognosis and Treatment.—The disease in children often disappears as the patient grows older. There is a possibility of successful treatment by attention to gastro-intestinal conditions and attempts to improve the general health. Arsenic has been known to lengthen the interval between attacks; but its long continued use is not to be recommended for so innocent a disease. Locally, irritating applications should be avoided. Bland mouth washes and painting with balsam of Peru or tincture of myrrh or benzoin may be used. Unna recommends an emulsion with sulphur in suspension to be painted on. Stelwagon obtained benefit from antacid laxatives. as calcined magnesia, given occasionally.

Ormsby has recently obtained cures by the application of radium, in moderate dosage lightly screened with silver.

Glossy Plaques.—**Synonyms.**—Plaques lisses. Smooth patches of the tongue.

Definition.—These are round or oval spots, pinhead to a centimeter or more in diameter, from which the papillæ have disappeared, leaving them with a dry, red, varnished appearance. They occur anywhere on the dorsum of the tongue and remain stationary for months or years, causing no pain.* These spots are sharply circumscribed, but have no differentiation of the border, as in the transitory benign plaques. They seem to be clinically indistinguishable from the syphilitic plaques lisses of Fournier and therefore can be diagnosed certainly only by the exclusion of syphilis. Darier calls attention to the resemblance of these plaques to the earliest lesions of leukoplakia.

Etiology.—Various causes for them are given, from nervous diseases, tuberculosis and diabetes to chronic indigestion and carious teeth.

Treatment.—Discovery and treatment of the cause of the disorder is, of course, the first indication. Locally, frequent painting with balsam of Peru and a bland mouth wash are recommended. Silver nitrate should not be used in view of the possibility of a beginning leukoplakia, in which any such superficial irritant is harmful. Radium or *x*-rays should be beneficial.

Leukoplakia.—**Synonyms.**—Leukokeratosis buccalis. Smokers' patches. Leukoplasia.

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* The cases described as painful glossy plaques are cases of Mueller's glossitis, a disease which occurs only in adults.

This disorder, so common in adults, is very rare in children, but does occur in them, and is of enough importance to warrant a brief discussion. Appearing first as red, denuded areas on the tongue, or as pearly, bluish or grayish-white spots on any part of the buccal mucous membrane, it gradually tends to thicken, sometimes forming wart-like growths, and often resulting in infiltration and inelasticity of the membrane, and consequent fissures. Only when fissured is it apt to be painful, though at other times well-developed lesions give a subjective sensation of stiffness. It occurs on the side or dorsum of the tongue, on the inner surface of the lips or cheeks, or upon the gums, less often upon other parts of the mouth. It may occur in the vagina, upon the inner surface of the labia or upon the glans penis. The lesions are usually round or oval patches, but on the cheeks between the opening of the jaws they are apt to be triangular, and on the tongue they are often longitudinal streaks. The borders may be sharply defined, smooth or jagged, or may fade gradually into the normal membrane, sometimes with increased redness of the adjacent membrane. The white, thickened epithelium sometimes scales off; but is usually quite adherent and on forcible removal leaves a raw surface. The disease progresses slowly until repeated fissuring or the growth of warty projections announces the danger of epithelioma, which is the frequent outcome.

Etiology.—Syphilis, tobacco and irritations due to jagged teeth or to the altered chemistry of the mouth in cases of pyorrhea are usually held responsible. Long-continued irritation is necessary to cause the condition, and this seldom begins early enough to result in leukoplakia until after puberty. Cases of slight degree do occur, however, in children in which none of the etiologic factors are evident. A careful examination for syphilis is always indicated in such a case, and in case of a negative result every effort should be made to discover other etiological factors.

Diagnosis.—The greatest difficulty is the differentiation between leukoplakia and mucous patches. The positive diagnosis of syphilis does not rule out a complicating leukoplakia. Only persistence of the lesions after anti-syphilitic treatment will settle the question, though persistence in one location, thickness, opacity and sharply defined borders point to leukoplakia. The smooth red areas of beginning leukoplakia cannot be differentiated from plaques lisses, with which, in fact, they may be identical.

Prognosis.—The danger of neglecting a leukoplakia should always be impressed upon the relatives or guardian of the patient. Darier mentions having seen carcinoma of the tongue with leukoplakia in a girl of 19. Prophylaxis, by avoidance of irritating foods and drinks, removal of irritation from jagged or carious teeth, etc., is by far the most important measure for the pediatrist. A soothing alkaline mouth wash should be used and the patches carefully dried and painted with balsam of Peru, tincture of benzoin or of myrrh, once a day or oftener. The condition of the digestive tract must be carefully regulated. Mild cases may yield to this treatment. Persistent ones should be given Roentgen or radium exposures sufficient to cause a sharp reaction, which usually results in a cure. Any destructive measure must be thoroughly carried out, and the use of silver nitrate or phenol is to be condemned as too superficial. The actual cautery or 20 per cent. chromic acid are efficient if care is taken to destroy the whole lesion.

Perlèche.—Definition.—An infectious disease of the labial commissures, occurring usually in children.

Symptoms.—It begins as a whitening of the mucous membrane and adjacent skin, extending a short distance within and without the mucocutaneous line. A mother-of-pearl appearance with wrinkling of the epithelial surface, is characteristic. It is nearly always bilateral when first seen, and seldom extends far from the points of origin. Later shallow fissures appear, converging at the labial angle, and seldom deep enough to cause bleeding. In severe cases the wrinkled, macerated surface epithelium exfoliates. There is rarely a slight reddening of the skin at the edge of the lesion, usually none. Subjective symptoms are limited to a sensation of dryness and burning, which causes the patient to lick the lesion. Sometimes it itches, and rarely causes pain as a consequence of the fissures formed by stretching the parts. It usually yields to treatment in a few weeks, but leaves the epithelium for months with a characteristic pearly appearance. Relapses are common. It never ulcerates in uncomplicated cases.

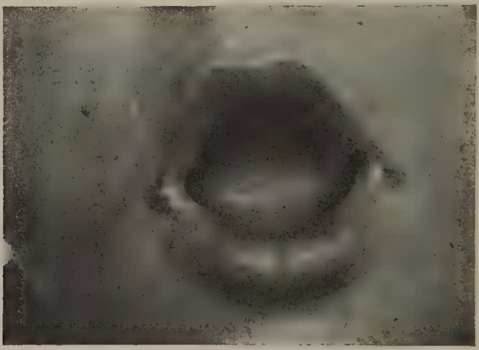

FIG. 84.—Perlèche, early case. (Collection of Dr. J. E. Lane.)

In Europe the disease is quite common. It was supposed rare in America until the recent paper of Lane, who reports 40 or 50 cases in New Haven.

Etiology.—Lemaistre, who first described the disease, found the streptococcus plicatilis in the lesion, and in wells, fountains and wooden drinking cups used by the patients. Later efforts to prove it of staphylococcic origin have not succeeded, and present opinion is in favor of the correctness of Lemaistre's findings.

Diagnosis.—Eczema of the labial commissures is often unilateral, may extend further on the skin with characteristic chapped appearance, lacks the whitish wrinkled appearance and causes much deeper, painful and bleeding fissures. It is usually much more resistant to treatment. The greatest difficulty is to distinguish perléche from the mucous patches so common at the labial commissures of syphilitic children. The characteristic white, wrinkled epithelium of perléche does not resemble a mucous patch, which is always an erosion; but on no less authority than that of Fournier, the diagnosis of perléche cannot be made definitely except by the exclusion of syphilis. Finding the spirocheta pallida settles the question; but the absence of this organism does not rule out syphilis. A negative Wassermann reaction is of greater value, but not absolutely incompatible with active syphilis. Of course with a positive Wassermann reaction, perléche may be present; but this is only of academic interest, as the case must be handled with regard to syphilis.

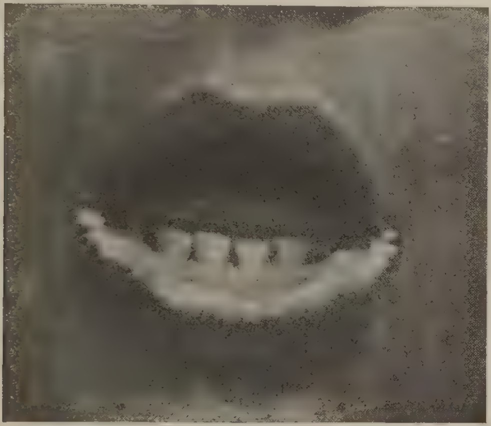

Fig. 85.—Perléche, well developed case. (Collection of Dr. J. E. Lane.)

Treatment.—The disease can be prevented by care to avoid the use of common cups and eating utensils, and the habit of sticking pencils, pins, etc., into the mouth. Kissing on the lips is also a common means of infection, and should be prevented.

Silver nitrate, 10 per cent., penciled on once a day, or a dilute tincture of iodin, will clear up most cases. Other antiseptic applications have been recommended, but these seem to be the simplest and most reliable.

Furrowed Tongue.—**Synonyms.**—Lingua plicata. Grooved tongue. Scrotal tongue. Wrinkled tongue. Ribbed tongue.

Symptoms.—Abnormal deepening of the furrows on the dorsum of the tongue is often a part of macroglossia, and though congenital, may not become marked until puberty. The furrows are usually arranged as a central longitudinal main furrow with side branches. The condition is of no importance except in the marked cases, in which the furrows need special cleansing to rid them of particles of food which might cause irritation on decomposition. Aside from this, the only importance attached to the disorder is to differentiate it from diffuse tertiary syphilitic glossitis, in which the furrows are irregular, the tongue is harder than normal, the mucous membrane is redder or paler than normal in certain areas, and appears stretched and nearly free of papillæ. The Wassermann reaction is usually positive, and leukoplakia may be present, while the stigmata of congenital syphilis, or even other active lesions, often assist in the diagnosis. Scars due to healed syphilitic or tubercular ulcer are easily recognized. Furrowed tongue causes no pain or discomfort and is of normal consistency.

Treatment.—No treatment, except cleanliness, swabbing out the furrows and the use of an antiseptic mouth wash, is necessary.

Black Tongue.—Synonyms.—Hairy tongue. Lingua nigra. Hyperkeratosis linguæ.

Definition.—An abnormal lengthening of the filiform papillæ, usually of a brown color.

Symptoms.—This rare malady occurs occasionally in children, but in them the color is more striking than the lengthened papillæ. Usually occurring in the center of the dorsum of the organ just in front of the circumvallate papillæ, it consists of an area in which are seen hair-like projections, black at the center, shading off to deep brown at the edges. The classic comparison of Raynaud is to the appearance of grain beaten down by a storm. It usually comes on gradually and lasts for weeks or years, then disappears spontaneously. No cause for it is known, the spores found by several investigators not being distinguishable from many found on normal tongues.

Exceptionally the discolored or hairy patch may be in other parts of the tongue, as behind the circumvallate papillæ, near the end of the tongue or on one side. Other colors, as yellow or blue, have also been observed. The hairy patch may be of normal color, or the colored area may not be hairy, as is frequent in children.

Treatment.—As the disease is benign, and usually self limited, no severe treatment is justified. Even after shaving off the hair-like filaments they have recurred. Mild cleansing and antiseptic washes are all that is indicated.

Cheilitis Glandularis.—Synonyms.—Cheilitis glandularis apostematosa. Myxadenitis labialis.

Definition.—A rare chronic inflammation of the lips with marked dilatation of the ducts of the mucous glands.

Symptoms.—The lips are usually somewhat swollen and slightly reddened, with occasionally an additional erythema of the adjacent skin and mucous membrane. The orifices of the mucous ducts gape and ooze a thick opaque secretion which sometimes dries to form crusts, or causes the lips to stick together in the morning. On pressure more of the fluid is easily forced out. The swollen glands can often be felt as nodules as large or larger than a hemp seed. It seldom occurs in children, and no cause is known. Some cases have yielded to potassium iodid internally, though they had no relation to syphilis. A chlorate of potash mouth wash and mild silver nitrate penciling was the local treatment in the successes of Volkmann, who first described the disease. Others have used black wash and glycerin, or *x*-rays, with more or less success.

Cheilitis Exfoliativa.—Definition.—A chronic crust formation upon the lips, with little swelling or redness and more or less tendency to fissure.

Symptoms.—This rare disease of the lips has been definitely placed as a part of seborrheic dermatitis by several authors. Other lesions of seborrheic dermatitis often accompany the disease of the lips, but not in every case. The lips, usually over the greater part of the surface, are constantly covered by thin scales or crusts, which cause discomfort or even pain when fissures result, as they often do. There is seldom marked redness, and the disease seldom extends beyond the lips, though involvement of the tip of the tongue in one case, and the inside of the cheek in another, have been reported. Sometimes the crusts become very thick, exfoliating rapidly and reforming. Picking off the scales, which is commonly done by these nervous patients, adds to the pain.

Treatment.—The disease is very resistant to treatment. Sulphur and salicylic ointments, resorcin lotions or ointments give the best result, but if apparently successful must be kept up, for the tendency to recur is great. *X*-rays and radium have been used with success, and Sutton reports a cure in one case by the use of carbon-dioxid snow.

Fordyce's Disease.—Definition.—A congenital abnormality manifested by more or less numerous white or yellowish points in the mucous membrane of the lips or cheeks.

Symptoms.—On the cheeks between the teeth or upon the upper lip or both lips is seen a surface closely stippled with tiny white or yellowish points, usually not raised above the surface, but sometimes slightly elevated. There is no abnormal redness nor any sign of a break in the surface. Where the lesions are very thickly set, they may be made to show more distinctly by stretching the tissue. There are no subjective symptoms except in rare instances in which slight burning or itching was mentioned. The condition does no harm and is of importance only when it causes disfigurement of the lips.

Etiology.—Fordyce, who described the condition, thought it due to a degeneration. Others have maintained that it is due to development of sebaceous glands. The latter has been shown by Margolies and Weidman to be the fact. They saw mild cases in 15 per cent. of children between two and nine years of age and in 26 per cent. of children between 9 and 14. No cases were found in 90 infants under two years old.

Treatment.—Fordyce obtained a temporary lessening of the lesions by scraping the surface and pressing out the yellowish bodies. Sutton recommends thorough freezing with carbon-dioxid snow.

Periadenitis Mucosa Necrotica Recurrens.—**Synonyms.**—Chronic aphthæ. Ulcus neuroticum mucosæ oris.

Symptoms.—A very rare disorder of the oral mucosa, beginning as a small, hard, smooth nodule deeply situated, which in three or four days enlarges and sloughs out as a necrotic plug, leaving a deep ulcer, which heals in about a week with the formation of a soft grayish irregular scar. The process is accompanied by moderate fever and such intense pain that eating is often impossible. The nodules are also tender. Usually one appears at a time, but sometimes there are two or three. The favorite locations are the sides and under surface of the tongue, but they may occur on the dorsum or on the lips or cheeks. Usually the disease begins after puberty, but Sutton's case began in infancy.

Etiology.—The etiology is unknown. Loblowitz, who first described it, believed it of angioneurotic origin. Histologic and bacteriologic study has shown nothing specific.

Treatment.—Local treatment has little effect. Sutton was successful in his case by hygienic measures, outdoor sleeping, light exercise, careful feeding, and cod-liver oil, iron, and arsenic.

Intraoral Herpes.—**Synonyms.**—Aphthous stomatitis. Canker sores.

Symptoms.—This disease is very common and seldom important except when severe or when its presence leads to a suspicion of syphilis. The term "aphthous" is a misnomer. A small vesicle appears on the inner side surface of the cheeks or lips, or on the tongue or gums, promptly breaks and leaves a round or oval erosion or shallow ulcer covered by a grayish pellicle, and often surrounded by a red zone. It is usually very tender, the slightest irritation causing a sharp burning pain. It may remain small and clear up spontaneously in a few days, or it may grow larger and deeper with sometimes some elevation of the border. There is often an accompanying edema of the tongue and cheeks, causing the child to bite its tongue or lips in chewing and adding to the pain. Severe attacks of this disorder are very distressing, making eating a torture.

Etiology.—The disease may be part of a disturbance elsewhere in the gastro-intestinal tract, as simple indigestion, constipation or some more severe disease, or it may be secondary to any febrile disease.

Diagnosis.—Thrush can be distinguished by the somewhat raised white patches which show the fungus under the microscope. Mucous patches are more superficial, less sharply defined, not surrounded by a red halo, and not tender. The spirocheta pallida can often be found in the serum from the mucous patch.

Treatment.—Touching the sores with 10 per cent. silver nitrate will usually stop the pain and result in prompt healing. Where this fails a small piece of alum held in contact until the surface is thoroughly puckered will often succeed. Correction of the gastro-intestinal disorder should prevent further attacks.

Bednar's Aphthæ.—These consist of oval erosions symmetrically placed upon the posterior part of the hard palate and the adjacent soft palate of newborn infants. Usually they cause no symptoms and yield to treatment within a few days. Sometimes they offer an opening for infection, which may cause destructive ulcers and lead to a fatal outcome. They are due to the over-zealous cleansing of the mouth, which injures the tender membrane, which at this place has little submucous tissue to cushion it. Greater gentleness in swabbing the mouth prevents this disease. Daily application of a 2 per cent. silver nitrate solution gives prompt relief of the condition when established. .

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CHAPTER CLXXXIX

EAR DISEASES IN CHILDHOOD

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Introduction.—By far the most precarious period for the ear in the life of an individual is during childhood. It is at this time that infections of the middle ear are most frequently encountered, owing largely to complications from the acute infectious diseases, and it is during this period, also, that most of the cases of destruction of the internal ear leading to deaf-mutism take place. For these reasons, a knowledge of the diseases of the middle ear, as well as of the labyrinth, is even more essential for the pediatrist than for the internist, whose practice mostly concerns adults. In order to grasp the significance of ear diseases, whether of the middle ear or of the labyrinth, it is essential that one possess a knowledge of the fundamental facts in the anatomy and the physiology of this organ.

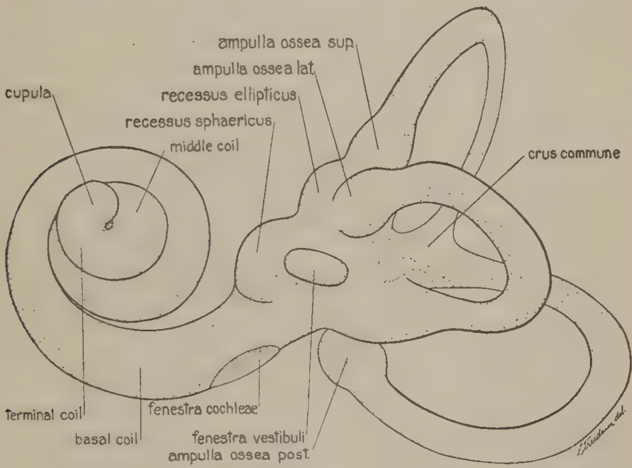

Fig. 86.—Wood's metal cast of the osseous cavities of the left labyrinth.

Anatomy.—**Internal Ear.**—The important part of the ear, as far as function is concerned, is the internal ear or otic labyrinth. This includes the mechanism which has to do with the perception of sounds, the acustic labyrinth, and another, which has to do largely with the preservation of the body equilibrium, the static labyrinth. The end organs which accomplish these functions are lodged in a membranous structure which is suspended in a complicated series of cavities in the petrous bone, the osseous labyrinth. The relations of the bony labyrinth are best seen in the Wood's metal casts of its cavities (Fig. 86). The cavities of the osseous labyrinth consist of a central chamber known as the vestibule, from the anterior end of which arises a spiral tube coiled upon itself in the form of a snail shell, making in man two and one-half coils. This is called the chochlea. From the opposite end of the vestibule arise three half-circle canals, the semi-circular canals. The cavities are lined with an endosteum and are filled with a fluid, the perilymph, which communicates through the aqueductus cochleæ with the fluid in the subarachnoid space.

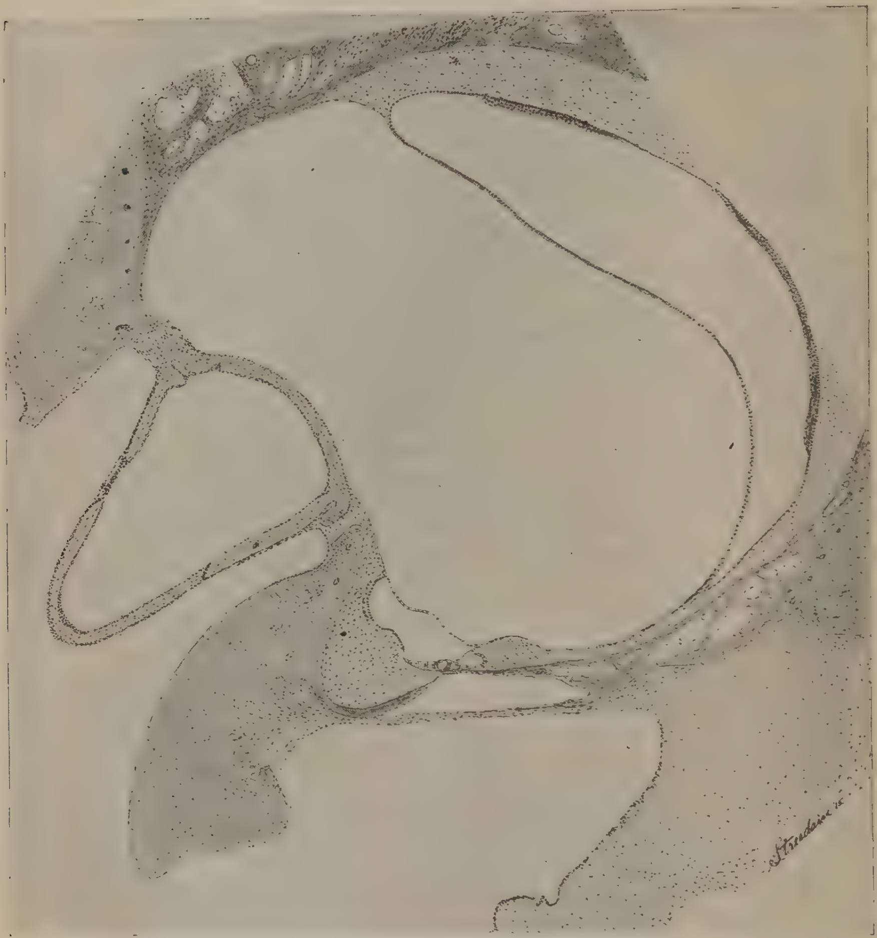

Fig. 87.—Section through the inner wall of the tympanic cavity of the pig's ear, showing articulation of stapes, section passing through promontory and round window showing membrana tympani secundaria separating tympanum from scala tympani of cochlea. The organ of Corti in the beginning of the basal coil is shown, as well as the macula acustica.

The important relations of the labyrinth to the neighboring parts are as follows: In the inner wall of the tympanum near the upper posterior part of the tympanic cavity is an oval window, the fenestra vestibuli, which opens into the vestibule and which is closed by the foot-plate of the stapes (Fig. 87). Just beneath this window the first turn of the cochlea makes a conspicuous prominence, the promontory. Immediately below and back of the promontory is a depression, at the bottom of which is a round window, the fenestra cochleæ, which opens into the scala tympani of the cochlea and is closed by the membrana tympani secondaria (Fig. 87). The apex of the cochlea lies just internal to the tympanic orifice of the Eustachian tube. The horizontal canal forms a prominence in the floor of the aditus ad antrum, while the superior canal makes an elevation on the upper border of the petrous bone in the middle brain fossa. The internal auditory canal for the passage of the seventh and eighth cranial nerves and the artery supplying the labyrinth opens on the posterior aspect of the petrous bone. A short distance from this opening is a small passage leading to the vestibule, the aqueductus vestibuli. It contains a small duct from the membranous labyrinth, the ductus endolymphaticus, which communicates with the utricle and saccule in the vestibule and opens into a small sac between the layers of the dura, the saccus endolymphaticus. On the same aspect of the petrous bone about midway between the internal meatus and the bulb of the jugular is another minute opening, which leads to the basal coil of the cochlea, the aqueductus cochleæ. It provides the communication between the perilymph which fills the osseous labyrinth and the fluid in the subarachnoid space.

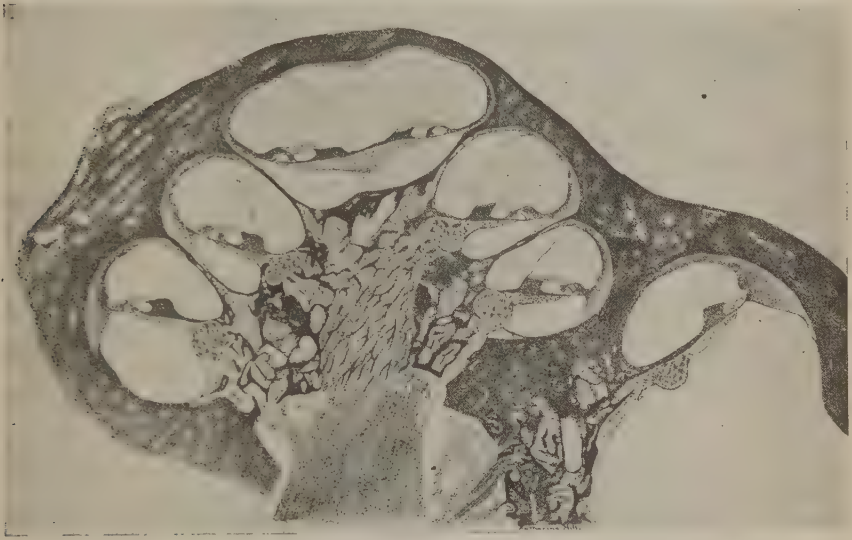

Fig. 88.—Cross-section through the cochlea of the pig.

The membranous labyrinth is made up of a series of communicating cavities suspended in the perilymph filling the osseous chambers. In the vestibule are two bags, called the saccule and the utricle. In the cochlea is an elongated tube which follows the spirals of the cochlea to its apex, the cupula. This is the ductus cochlearis, also known as the scala media (Fig. 88). In each of the semi-circular canals is a membranous tube which opens at either end into the utricle. At one end of each membranous canal is an expansion called the membranous ampulla.

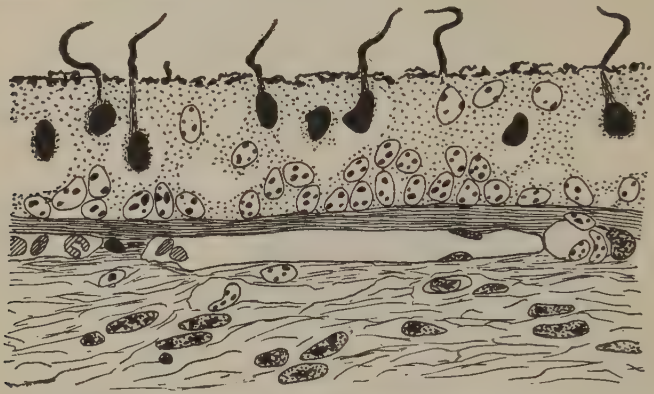

FIG. 89.—Section through the macula acustica.

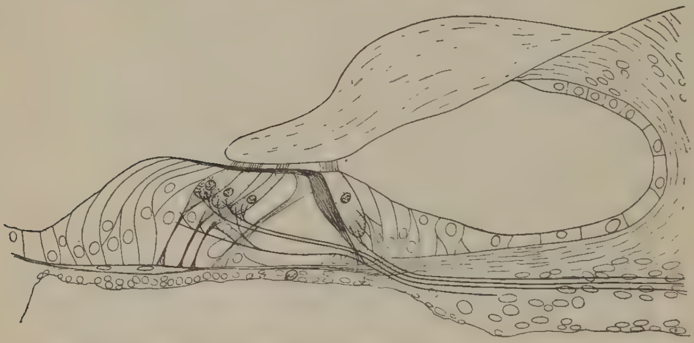

FIG. 90.—Section through the organ of Corti. Terminal filaments of the cochlear nerve are semi-schematic.

In the membranous labyrinth are located three types of end-organs which receive the terminal filaments of the eighth nerve. In the vestibule is located one type, the macula acustica of the utricle and saccule (Fig. 89). In the cochlea is the second type of end-organ, the the organ of Corti (Fig. 90). The semi-circular canals house the third type of end-organ, the crista ampullaris, of which there is one for each canal located in its ampulla (Fig. 91).

Histologically, these three types of end-organs are quite similar, although at first glance they may appear quite unlike each other.

In each the important physiological element is a peculiar hair-bearing cell which receives the terminal filaments from the eighth cranial nerve. Superimposed above the hair cells in each end-organ is a peculiar structure of epithelial origin. In the macula acustica this is the otolith membrane, in the organ of Corti it is the membrana tectoria, and in the crista ampullaris it is the cupula. Another anatomical fact which has an important bearing on the physiology of these end-organs is that in each the hairs of the hair cells are in actual contact with and adherent to the under surface of its superimposed membrane. It is quite clear from an examination of the anatomy of these end-organs that their reaction to stimuli must be much the same as will be discussed under the physiology.

The eighth nerve which supplies the labyrinth of the ear is in reality two nerves which have a separate central origin and a different peripheral distribution. The cochlear portion supplies only the organ of Corti and has to do solely with the function of hearing, while the vestibular portion supplies the macula and crista acustica and has to do with the function of equilibrium and the sensing of motion.

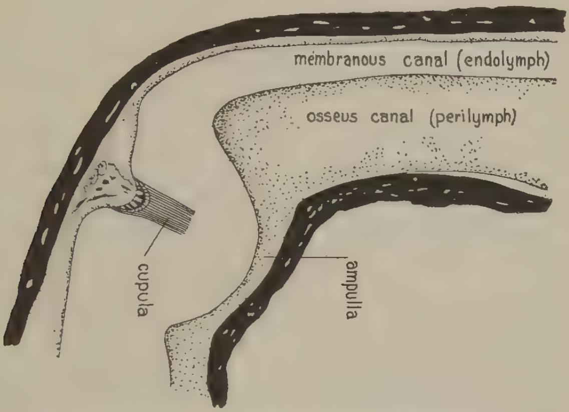

FIG. 91.—Section through the semi-circular canal showing relation of membranous to osseous canal, the ampulla and its crista acustica.

The blood supply of the labyrinth is through a single vessel, a branch of the basilar artery, which enters the labyrinth by way of the internal meatus. The venous blood leaves the labyrinth for the most part through a vein which runs along the aqueductus cochleæ. Not infrequently a small vessel leaves along the aqueductus vestibuli.

Middle Ear.—The middle ear is made up of a series of communicating pneumatic spaces which begin with the pharyngeal orifice of the Eustachian tube in the lateral wall of the nasopharynx and terminate in the adult in the pneumatic spaces of the mastoid process. In the newborn the middle ear consists of the Eustachian tube, the tympanic cavity with its antrum and a communicating passage called the aditus. The mastoid process does not exist. It is only as the child begins to develop and the need for a firmer attachment for the sternomastoid muscle arises that the mastoid process develops, and it is not until about the age of puberty that the pneumatization of the process is completed.

The Eustachian tube has a flaring trumpet-shaped opening in the lateral wall of the nasopharynx. The location of this opening is such that it is readily pressed upon by an enlargement of the pharyngeal tonsil, adenoid vegetations. Its course is upwards, backwards and outwards to the tympanic cavity, into which it opens by a flaring orifice in the anterior wall of this chamber. The inner two-thirds of the tube is membranous and cartilaginous; the outer third is osseous. A constriction, the isthmus, exists in the osseous portion near its junction with the membranous part. The tube is lined with ciliated epithelium. The osseous portion is open, while the membranous portion is closed except as the act of swallowing dilates the tube and allows the passage of air into the tympanum. With the pneumatization of the mastoid it is not uncommon for similar pneumatic spaces to develop in the osseous portion of the tube near the tympanic orifice, producing socalled tubal cells.

The tympanic cavity is made up of three parts: The meso-tympanum or tympanic cavity proper, the recessus epi-tympanicus made up of the attic and the aditus, and the recessus hypo-tympanicus, a depression lying below the level of the attachment of the membrana tympani. The outer wall of the tympanum proper is made up of the membrana tympani or drum membrane, while the outer wall of the attic is formed by a shelf of bone forming the upper wall of the external meatus and by Shrapnell's membrane. The upper wall of the tympanum is a thin shelf of bone called the tegmen, which extends over the attic, the aditus and the antrum. The petro-squamosal suture passes through this tegmen, and in the child free blood-vessels and lymphatic connections exist between the dura of the middle brain fossa and the mucous membrane of the middle ear. The floor of the tympanum in children is in close relation to the bulb of the jugular so that the direct extension of infection from the middle ear to the bulb may readily take place. Even in adults the bulb not infrequently encroaches on the floor of the tympanum, where it may be seen as a dome-like prominence and may even be exposed through dehiscence of the bony covering. The orifice of the Eustachian tube is in the upper half of the anterior wall of the tympanum. The median wall of the tube at this point is separated from the internal carotid by a very thin bony plate. The upper half of the posterior wall of the tympanum is occupied by the opening into the antrum, the aditus. The inner wall of the tympanum separates this cavity from the labyrinth. It is perforated by two windows which lead to the labyrinth. Opposite the upper posterior quadrant of the membrana tympani is the oval window for the footplate of the stapes, the fenestra vestibuli, and opposite the lower posterior quadrant is the niche for the round window, the fenestra cochleæ, closed by the membrana tympani secondaria, which separates the cavum tympani from the scala tympani of the cochlea. Beginning between these two windows and extending toward the middle of the inner wall of the tympanum is the promontory, a prominence produced by the first turn of the cochlea. The canal for the facial nerve runs horizontally across this wall of the tympanum. The nerve enters the cavum tympani in front of the oval window and runs backward just above this opening until it reaches the posterior wall of the tympanum, when it turns directly downward, lying in the posterior wall of the external meatus, a little external to the level of the inner wall of the tympanum, to emerge through the stylo-mastoid opening. This opening in the newborn lies on the outer aspect of the petrous bone, about the level of the floor of the tympanum (Fig. 92). After the mastoid process develops, this opening is obscured behind this process.

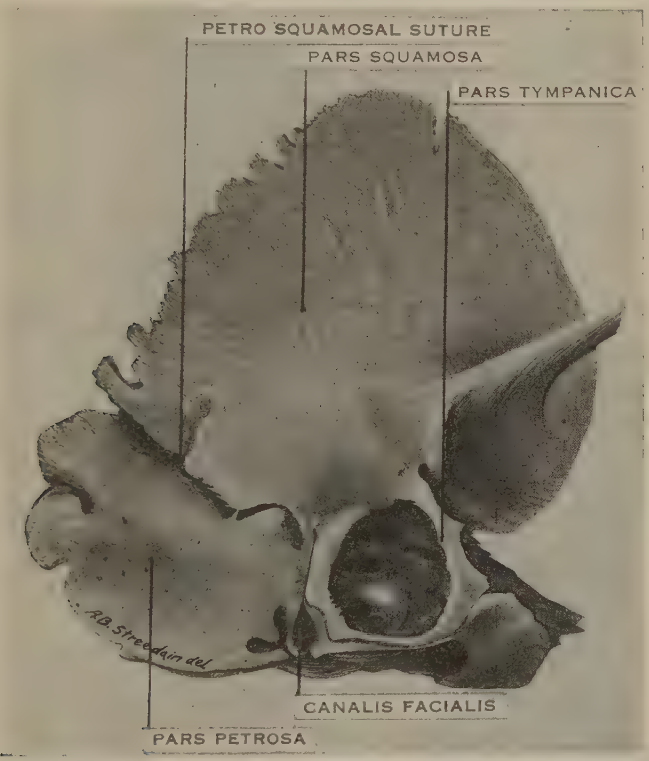

Fig. 92.—The temporal bone in a new-born child. Note the absence of a mastoid process and osseous external meatus, the persistence of the petro-squamosal suture and the opening of the facial canal.

A chain of three small ossicles, the malleus, the incus and the stapes, connects the drum membrane with the oval window. The malleus is attached to the drum membrane, while the foot-plate of the stapes is attached by a circular membrane in the fenestra vestibuli. This constitutes the sound-conducting mechanism. Most of the malleus and the incus lie in the attic. Folds of mucous membrane connect these ossicles with the walls of the tympanum and with each other. These membranes often separate the attic from the tympanum proper except for a small passage, and they often extend over into the antrum. They form the basis for the formation of thickened adhesive bands, causing fixation of the sound-conducting mechanism in the so-called chronic adhesive middle ear catarrh.

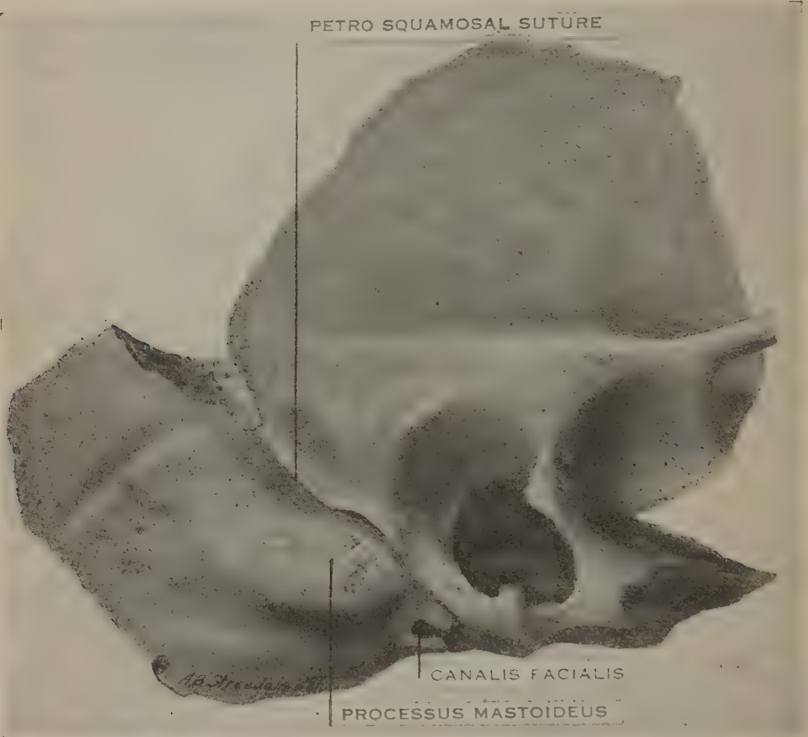

Fig. 93.—Temporal bone of a child at the end of the first year. Note the developing mastoid process and osseous external meatus, the location of the opening of the facial canal and the persistence of the petro-squamosal suture.

In the newborn child the tympanum and antrum are filled with a gelatinous thickening of the mucous membrane lining these cavities. It is only after the child has dilated the Eustachian tube through the act of nursing that air is allowed to enter the tympanum and the atrophy of this thickened membrane takes place, allowing these chambers to become pneumatic. This period does not last over a few days.

The roof of the antrum is formed by an extension of the tegmen separating the attic from the middle fossa. In the floor of the aditus is a prominence caused by the horizontal semi-circular canal. Immediately in front of this prominence lies the canal for the facial nerve. The outer crus of the superior semi-circular canal lies close to the inner wall of the aditus.

The mastoid process does not exist in the newborn. The three parts which go to make up the temporal bone are easily separated in the infant's skull. The petrous bone which encloses the labyrinth is surmounted by the pars squamosa, which forms the covering for the antrum and the attic. The suture between these two parts passes through the tegmen as well as through the outer wall of the antrum (Fig. 92). The tympanic bone forms but a partially complete rim, which serves for the attachment of the membrane tympani. The membranous external meatus in the newborn is attached directly to this bony rim. At the end of the first year the mastoid process has already begun to form as a nipple on the outer aspect of the petrous bone (Fig. 93). An osseous external meatus has also begun to form, especially the posterior wall formed by the mastoid and the upper wall formed by the pars squamosa. The anterior lower part of the canal is still open. The petrosquamosal suture passing through the outer wall of the antrum is still quite distinct. At the age of three a mastoid process has formed, as has the osseous external meatus, although both have by no means reached their full proportions. In the adult the mastoid process forms the posterior upper wall of the external meatus, the tympanic bone forms the anterior and lower wall, while the pars squamosa closes in the remaining segment above. No evidence of the petrosquamosal suture is to be found in the adult except occasionally as an anatomical variation.

External Ear.—The external ear comprises the auricle and the external meatus. It differs materially in the newborn from the external ear of the adult. The cartilage of the auricle is very soft and pliable and the characteristic outlines are considerably less distinct. The external meatus is very much contracted and consists only of the membranous cartilaginous portion, which is attached directly to the bony ring formed by the os tympanum.

In the newborn child the external meatus is filled with epithelial cells, which only after several weeks are thrown off and extruded together with the secretion and expulsion of cerumen.

The direction of the membranous external meatus is somewhat upward, backward and inward, whereas the bony meatus, when it forms, is directed more downward, forward and inward. In order to get a satisfactory view of the drum membrane, it is necessary to seize the upper rim of the auricle and pull it gently upwards and backwards, thus straightening out the angle between the membranous and bony portions. In the membranous portion of the external meatus are glands secreting cerumen, and in this part of the meatus are small hairs.

Physiology.—The labyrinth of the ear has two quite distinct functions, the function of sound perception, in the acustic labyrinth, and the function of sensing motion with that of preserving the body equilibrium in the static labyrinth. The acustic labyrinth is restricted to the distribution of the cochlear nerve and is located solely in the cochlea. The static labyrinth is limited to the distribution of the vestibular nerve and is located in the vestibule and semi-circular canals.

Function of the Cochlea.—Two conceptions have long been accepted as fundamental in the theory of sound perception. One is that this is dependent on the physical vibration of structures in the cochlea in response to impulses from the outer air. The other is that the perception for the several tones in the scale takes place in separate and distinct parts of the cochlea. Before the discovery of a membranous labyrinth the bony plate which extends as a shelf part way across the cochlear tube, the lamina spiralis ossea, was believed to be the vibrating mechanism which responded in one part to tones of a certain pitch and in another part to tones of a different pitch. With the discovery of the organ of Corti it became clear that the perception of sound is dependent on the stimulation of the hair cells of Corti's organ, which receives the terminal filaments of the cochlear nerve. Helmholtz accepted the two pre-existing fundamental conceptions regarding the perception of sound. He selected the basilar membrane on which Corti's organ rests as the vibrating structure and with this anatomical basis worked out the theory of sound perception in great elaboration. According to his theory, the perception for the tones in the upper part of the scale takes place in the basal coil and that for the lower tones toward the apex of the cochlea. Vibration in separate parts of the basilar membrane depending on the pitch of the tone would result in the stimulation of separate groups of hair cells for each tone by carrying the cells upward and brushing their hairs against the under surface of the membrana tectoria, which was supposed to lie a short space above the projecting hairs. Several modifications of the basilar membrane theory of sound perception have been suggested. Max Meyer suggests that the highest notes produce vibrations in only the beginning of the basal coil and that each tone lower in the scale causes a larger and larger part of this membrane to vibrate. In this way a different grouping of hair cells would be stimulated for each tone in the scale. The lowest tones would thus cause the whole of the membrana basilaris to vibrate, stimulating all the hair cells throughout the cochlea. Ewald imagined that each tone produced vibrations in the whole extent of the basilar membrane but that these vibrations would necessarily differ for each tone of the scale. Only those hair cells would be stimulated which occupied the crests of these undulations, and in this way separate groups of hair cells would be stimulated for each tone in the scale. Ewald's theory is based on the assumption that the membrana tectoria is separated by an appreciable space from the hairs of the hair cells.

In 1907 I first called attention to the fact that the hair cells in Corti's organ bear the same relation to the membrana tectoria as do the hair cells in the macula and crista acustica to their superimposed membranes, the otolith membrane and the cupula respectively. The relation is one of actual contact. This anatomical fact has since been verified by other anatomists. At this time I pointed out that the close structural analogy between the three types of end-organs found in the labyrinth indicated very clearly that their response to stimuli is probably very similar and that since the stimulation of the hair cells in both the macula and the crista acustica is dependent on the movement of the superimposed structures, the otolith membrane and the cupula respectively, it seemed probable that the stimulation of the hair cells in the organ of Corti is dependent on the vibrations not of the basilar membrane but of the membrana tectoria. Later I pointed out certain anatomical conditions, as, for example, the blood-vessels attached to the membrana basilaris under the tunnel of Corti, which made it impossible for this membrane to act as the vibrating mechanism in sound perception. To fill its rôle this structure must vibrate the same at all times to the same impulse. The theory of sound perception as modified by these facts is somewhat as follows: The tones higher in the scale produce vibrations in limited areas of the membrana tectoria near the beginning of the basal coil where this membrane is very small. These vibrations stimulate a certain group of hair cells, the impulses from which give the perception for those particular tones when transferred to the cortical centers. The lower tones produce vibrations in the membrana tectoria towards the apex of the cochlea where this membrane is found to be much larger, and, thus, stimulate other groups of hair cells. With this conception of tone perception we can readily account for the fact that disease of the labyrinth may result in destruction of hearing for certain tones in the scale, while the perception for the other tones is still preserved.

The Function of the Vestibule and Semicircular Canals.—The sensing of motion is a function of the end-organs in the vestibule and semicircular canals. The macula acustica of the utricle and saccule gives us our sense of motion in a direct line, while the crista acustica of the semicircular canals gives us the sense of turning motions. Besides this sensing of motion, the vestibular mechanism plays an important rôle in preserving the body equilibrium. It does this by virtue of tonus impulses to the skeletal muscles, which keep these muscles in a constant state of stimulation. The tonus impulses from the right labyrinth stimulate for the most part those muscles which produce movement towards the left, and *vice versa*. When one labyrinth is destroyed the patient will suffer from severe vertigo and will tend to fall towards the side of the injury due to the tonus impulses from the normal labyrinth acting without the restraint of opposing impulses from the affected side. The eyes will also be drawn over to the affected side, only to be jerked quickly back to the opposite side, constituting a nystagmus. These disturbances of equilibrium caused by the destruction of one labyrinth disappear in from a few days to a few weeks as the result of an adjustment of tonus to take the place of impulses from the destroyed labyrinth.

Function of the Sound-conducting Mechanism.—Both the external and middle ear have to do with the collection of sound waves from the outer air and their conduction to the labyrinth. The auricle in man plays a much less important rôle as a collector of sound waves than does this organ in many of the lower animals. Sound waves from the outer air produce vibrations in the durm membrane, which in turn transmits them along the chain of ossicles to the foot-plate of the stapes and thus to the fluid in the labyrinth. Sound waves from the outer air reach the inner ear, also, by direct conduction through the bones of the skull, that is, indirectly to the drum membrane and ossicular chain. Complete occlusion of the external meatus, either as the result of acquired or congenital atresia of this canal, produces only a partial loss of hearing so long as the internal ear remains intact. A destruction of the membrana tympani and of the ossicular chain results in only a very moderate depression of the hearing function so long as the movement of the stapes is unimpaired. On the other hand, fixation of the stapes always results in a profound depression of hearing by air conduction, but in these cases there develops with the loss of hearing by air conduction an increased hearing by bone conduction, which may be the result of a more ready transference of vibrations from the skull to the stapes.

DISEASES OF THE EXTERNAL EAR

Congenital Anomalies in the Auricle and External Meatus.—A great variety of developmental anomalies occur involving the several parts of the auricle as well as the external meatus. The auricle in makrotia is larger than normal in all its parts. This condition is usually symmetrically developed on the two sides. Largely because of its unusual size the ear stands out conspicuously from the side of the head. As a rule, this condition can be improved by surgical measures undertaken to reduce the size of the auricle and to correct the prominence of the organ.

Congenital mikrotia of the auricle is more common and is usually associated with a partial closure or even complete atresia of the external meatus. The degree of mikrotia varies from a defect in development of single parts of the auricle to its complete absence. Congenital development of supernumerary cartilaginous tags, especially in the region of the tragus, is quite common. Some of these conditions can be improved by surgical measures, but efforts directed to this end are not infrequently followed by scar formations, which in no way constitute an improvement over the original condition.

Congenital atresia of the external meatus is often associated with development anomalies involving the auricle as well as the middle ear. The latter include closure of the Eustachian tube, contraction in the size of the tympanum and the antrum associated with anomalies in the development of the ossicular chain, and sometimes complete bony occlusion of the labyrinth windows. In relatively few cases is this condition associated with defective development of the internal ear. On the other hand, congenital deafness is the result of developmental defects limited as a rule to the labyrinth itself.

The symptoms resulting from an atresia of the external meatus are limited to the defect in hearing, although adults will occasionally complain of a sense of fullness in the head. When the atresia of the external canal is not associated with involvement of the inner ear, the defect in hearing is by no means complete. The patient can hear the conversational voice sometimes as far as several meters. The functional tests disclose the typical reactions of obstructive middle ear deafness. In some cases these reactions are associated with a more or less extensive defect at the upper end of the tone scale, such as we might expect from an involvement of the basal coil which goes to form the promontory.

The treatment of this condition is not so simple, since it is scarcely possible to make a patulent external meatus down to the drum membrane. One can sometimes improve the hearing by a plastic operation to make a permanent opening into the antrum. Where the atresia is unilateral it is not necessary to undertake such an operation as the patient relies on the normal ear for hearing. As a matter of fact, this operation is rarely undertaken except in connection with an operation to relieve a mastoid abscess, which is prone to develop in those cases where infection extends to the tympanic cavity through a patulent Eustachian tube.

Acquired atresia of the external meatus which is the result of extensive ulceration or exostoses forming as a complication of chronic middle ear suppuration as a rule can be corrected by a plastic of the mastoid such as one employs when performing the radical mastoid operation. The mere excision of the scar formation in the external meatus is not sufficient to cure such cases.

Foreign Bodies in the External Meatus.—This condition is especially frequent in early childhood, when the foreign body is carried to the ear by the patient itself. It is important to keep in mind the fact that the harmful results of foreign bodies in the external meatus, with very few exceptions, arise from efforts directed towards their removal. An undisturbed foreign body lodges, as a rule, in the outer membranous part. It is only when instrumental measures have been employed that they are pushed beyond the isthmus of the canal, which lies just internal to the junction of the membranous with the osseous portion.

Most foreign bodies can be removed by sufficiently forceful syringing. When one has to deal with a live insect, a few drops of alcohol may be dropped into the ear before syringing. The removal of foreign bodies by means of instruments is a delicate and by no means simple procedure. It requires usually considerable skill in the manipulation of instruments under reflected light in this narrow canal. Various blunt as well as sharp hooks and pincettes are employed for this purpose.

Eczema of the Auricle and External Meatus.—Eczema of the external ear is especially frequent in early childhood, where it occurs in all its various forms of acute and chronic, moist and dry eczema. It is not infrequently a part of a general eczematous condition, but it is often the result of a suppurative discharge from the middle ear or of a furuncle in the external meatus. The most annoying symptom is the itching, which causes headache and fatigue when severe, and may give rise to various nervous symptoms when prolonged. In chronic cases the discharge from the ear is often foul smelling and purulent.

The **diagnosis** is not difficult as a rule. The condition must be differentiated from herpes of the auricle, which develops with marked burning and often with severe pain, and from phlegmonous perichondritis, which is a very painful affection associated with fever. The question of whether the eczema is secondary to a suppurative otitis media is not always easy to determine. A mucous discharge, of course, can come only from the middle ear. The defect in hearing is much more marked where the eczema is a complication of an otitis media.

The **treatment** is often a much as correction of general conditions, such as a faulty diet, as it is local. The latter must be varied to suit the case. Cleansing with water must be avoided. The secretion must be removed with pledgets of dry cotton. Alcohol is rarely tolerated. Salves of boric acid, zinc or mercury made up in lanolin rather than vaseline are most useful. Sometimes insufflation of powdered boric acid, after a careful drying of the canal, is useful. Very often the application of silver nitrate in 1 to 10 per cent. solution on a cotton pledget is the best means to employ.

Furunculosis of the external meatus occurs frequently in association with furunculosis elsewhere on the body. It occurs also as a complication of a local process, either of an eczema of the external meatus or of a purulent discharge from the middle ear. The furuncle is always located in the outer membranous portion of the meatus where the hairs are located, never in the inner osseous canal. The diagnosis is readily made by inspection of the meatus, which can be carried out, as a rule, without the use of an ear speculum. A furuncle must be differentiated from phlegmon of the auricle by the usual complete absence of temperature elevation in furunculosis. In deep-seated furuncle of the canal, a swelling back of the ear may push the auricle forward, producing a condition similar to that of a subperiosteal abscess in acute mastoiditis. From the latter the diagnosis must be made by the absence of symptoms of otitis media, such as elevation of temperature and a more marked depression of hearing. When a small speculum can be introduced, it will be possible to make an inspection of the drum membrane.

The **treatment** in the early stages is always conservative, instillation of 5 per cent. carbol-glycerine and the application of warm moist bandages. When the furuncle has developed a distinct "head," an incision with a thin sharp scalpel, such as the ordinary cataract knife, pushed in through the base and cutting out to the surface gives immediate relief. Where a tendency to recurring furunculosis develops treatment by autogenous vaccin is often of great value.

DISEASES OF THE MIDDLE EAR

Middle ear disease constitutes the most frequent form of ear trouble in childhood. The diagnosis of these conditions is based largely upon changes found by an inspection of the drum membrane. It is important, therefore, for one to be able to recognize the normal membrana tympani as well as the pathologic changes in this membrane.

The membrana tympani is slightly oval in outline. At the upper pole is a small indentation in the superior wall of the external meatus, the Rivini segment. Normally the membrane has a pearly-gray color and presents several conspicuous landmarks. Near the upper anterior margin is a small pointed elevation produced by the processus brevis of the malleus. Extending downwards and backwards from this point to the middle of the membrane is seen a line produced by the handle of the malleus, the manubrium, where it is embedded in the drum-membrane. From the lower end of the manubrium extending downward and forward is perhaps the most conspicuous landmark of the normal membrane, the cone of light. From the processus brevis to the lower angle of Rivini's segment, both in front and behind, are two more or less indistinct folds which mark the line of separation between the pars tensa, which lies below, and the pars flaccida, which lies above. The pars tensa is made up of an outer layer of epidermis and an inner layer of mucous membrane. Between these two is a strong fibrous layer made up of circular and radiating fibers arranged much as are the meshes of a spider web. The pars flaccida, or Shrapnell's membrane, has the outer and inner layers but lacks largely the middle fibrous layer.

In the more transparent membranes one can recognize the following structures shining through from the tympanic cavity. In the upper posterior quadrant is seen the long process of the incus as it extends downwards from the attic to articulate with the head of the stapes. Extending backwards from the point of articulation with the stapes and forming a right angle with this process of the incus is seen the tendon of the stapedius muscle. Shining through the lower posterior quadrant can be seen the niche for the round window. The rounded elevation of the promontory is recognized just above the depression for the round window extending forward to the middle of the membrane. Through the upper anterior pole of the pars tensa is seen the tympanic orifice of the Eustachian tube.

Catarrhal Diseases of the Middle Ear.—Under the term catarrhal diseases of the middle ear are included a variety of pathological changes characterized by more or less swelling of the mucous membrane and the outpouring of a serous or mucous exudate. Various terms are applied to these conditions, depending on the more conspicuous pathological changes, such as acute tubal catarrh, acute catarrh of the tympanum, acute tubo-tympanic catarrh, subacute middle ear catarrh, chronic tubo-tympanic catarrh, and chronic adhesive middle-ear catarrh. The conditions are, for the most part, secondary to pathological changes in the nasopharynx.

Acute catarrh of the *tube* and of the *tympanum* develops secondary to acute inflammatory changes in the nasopharynx, such as go with any ordinary head cold. The swelling of the mucous membrane in the Eustachian tube causes in most cases a temporary closure of its lumen. The absorption of the air confined in the tympanum leads to more or less retraction of the drum-membrane, and the development in the tympanum of an exudate which in part is the secretion of the glands in the Eustachian tube drawn into this chamber by suction and in part the secretion of the mucous membrane lining the tympanum.

The symptoms arising from these changes are depression of hearing with sensations of fullness and occasionally tinnitus. There is no pain caused by the changes in the ear and no elevation of temperature.

The diagnosis is readily made by inspection of the drum-membrane. When tubal occlusion is present the membrane is found in a strongly retracted position. The exudate in the tympanum produces changes which can be detected. The most conspicuous is a more or less increased transparency of the membrana tympani, associated with a characteristic yellow or straw color from the exudate shining through. When the fluid only partially fills the tympanum, a line of demarcation between the fluid below and the air above can be made out as a line resembling a hair lying across the membrane.

Subacute recurring catarrh of the middle ear is for the most part dependent on the pressure on the tubal orifice from enlargement of the pharyngeal tonsil, adenoid vegetations. It is characterized by marked retraction of the drum-membrane and by a more or less pronounced depression of the hearing function, which is prone to undergo rapid alterations brought about by alternating closure of the Eustachian tube and the occasional entrance of air into the tympanum, brought on by forcible blowing of the nose, sneezing, or even by the act of swallowing. The secretion of the tympanum in these cases is usually more mucous in character.

Chronic Catarrhal Otitis Media.—The more chronic forms of middle ear catarrh lead to changes in the tympanum which are permanent, producing the condition which is known as chronic adhesive middle ear catarrh. The sound-conducting mechanism is bound down by permanent adhesive bands, which have as their foundation for the most part the normal folds of mucous membrane connecting the ossicles with each other and with the walls of the tympanum. The drum membrane is fixed in a retracted position. Its lustre is diminished, and areas of thickening or of atrophy are conspicuous.

The **prognosis** in the several forms of middle ear catarrh varies widely. The more acute cases usually make a complete recovery with a return of the hearing to normal. The same may be true for the subacute forms, provided the cause is corrected by timely removal of the offending tonsils and adenoids. The chronic adhesive cases represent permanent changes from which recovery is not possible. In these latter cases improvement under treatment is seldom seen, even after the removal of enlarged tonsils and adenoids.

In the **treatment** of middle ear catarrh it should be remembered that the more acute cases recover spontaneously after the subsidence of the acute inflammatory condition of the nose and pharynx. Inflation in these cases is as likely to do harm by carrying infection into the tympanum and changing the middle ear process to a suppurative one as it is to benefit the case. The more subacute cases often clear up spontaneously in a few weeks after the tonsils and adenoids have been removed. When the tubal occlusion persists, inflation by the Politzer method two or three times a week for several weeks should be carried out. In those cases where the fluid in the tympanum persists, paracentesis, followed by expulsion of the fluid by inflation, usually brings the process to a speedy termination. In the more chronic cases every care should be taken to correct, as far as possible, any condition in the nose or pharynx which would tend to keep the process active. The most benefit can be expected from the removal of adenoids and tonsils. The latter may constitute a distinct menace to the ear, even when they are not enlarged, by constituting a focus of chronic infection from which frequent acute attacks of nasopharyngeal inflammation develop. In the treatment of such cases, too much importance has often been attributed to the correction of anatomical variations, such as the irregularities in the nasal septum so commonly met with. It may be possible for a deflected nasal septum to contribute in the causation of chronic middle ear catarrh, but it seems very doubtful whether this occurs except in those cases where the deflection is marked enough to produce an obstruction in nasal respiration sufficiently annoying in itself to justify its correction. Inflation in these chronic adhesive cases is of no special benefit except as it may be carried out over short periods from time to time, to relieve acute exacerbations of the conditions.

Acute Simple Middle Ear Inflammation, Otitis Media Serosa.—This form of middle ear inflammation is characterized by a swelling and reddening of the mucous membrane of the tympanum and by the outpouring of a serous exudate filling this cavity. The condition is one which in a short period clears up entirely with a return to normal. It is caused, as a rule, by extension of infection from the nasopharynx up through the tube but may be brought on as the result of a traumatic rupture of the membrana tympani. Infection through the tube is often the result of sneezing, too forcible blowing of the nose, the act of vomiting, or irrigation of the nose. The symptoms at the onset are not unlike those of acute suppurative otitis media except in severity. In the simple serous otitis media pain at the onset is a conspicuous symptom associated with fever, which may show a marked elevation in the young child. There is more or less marked depression of the hearing which, with the elevation of temperature, serves to differentiate this condition from the simple inflammation of the drum-membrane, primary myringitis.

The appearance of the drum-membrane is quite characteristic. The membrane is congested with an obscuring or obliteration of the normal landmarks, especially the light reflex and the line for the handle of the hammer. In influenza the formation of blood blisters over the drum-membrane and the neighboring wall of the external canal is quite characteristic. It should be remembered that in young children the drum-membrane is thicker and more resisting than in the adult, so that the usual bulging of the drum-membrane from the accumulation of fluid in the tympanum takes place less readily. For the same reason the membrane is less transparent and, therefore, does not present so readily the yellowish appearance from the fluid in the tympanum. In most cases the reaction in the middle ear is a diffuse process involving the mucous membrane of the attic as well as of the meso-tympanum. In exceptional cases the process is more circumscribed when it may be confined to the meso-tympanum or to the region of the attic, as evidenced by changes restricted to the pars tensa of the drum-membrane or to the pars flaccida, as the case may be.

The duration of the disease is from a few days to ten days at the most. As a rule, the pain disappears after the first day, and the absorption of the fluid is complete in the course of one week. In some cases there may persist certain permanent changes in the drum-membrane, such as diminution of luster and evidences of thickening, which must be interpreted as an indication of similar changes in the mucous membrane lining the tympanum. In such cases the recurrence of the acute process may readily produce permanent changes in the tympanum, leading to the development of the chronic adhesive middle ear processes.

The **treatment** in the beginning should be conservative. To quiet the pain instillation of a few drops of warm 5 per cent. carbol-glycerine may be used. Application of heat is usually very grateful. This may be in the form of an electric pad or the hot-water bag, care being taken to keep the rubber covered with a cloth to avoid risk of blistering the skin. Still more effective is the application of hot moist dressings, which should be covered by a piece of oiled silk and secured by a suitable bandage. Rest in bed and administration of a laxative should be carried out. The question of paracentesis is not always an easy one to decide, especially as it is difficult to make a sharp differentiation in some cases from the purulent otitis media. In all doubtful cases it is better to perform the paracentesis which can lead to no harm if carried out in the proper manner. If it is deferred in cases of purulent otitis media, which need drainage, the situation may be fraught with the risk of serious, even fatal, complications. After paracentesis has been done, care should be taken not to carry infection from the external meatus into the middle ear. For this reason irrigation of the external meatus should be avoided. Pledgets of cotton twisted out to a point or narrow strips of gauze should be placed in the external meatus and changed as often as they become saturated. This is the only local treatment after the opening of the drum-membrane except the application of heat in some form to ease the pain and to facilitate the free escape of discharge.

Acute Purulent Middle Ear Inflammation.—Acute middle ear suppuration is one of the most frequent diseases of childhood. The infection takes place usually as an extension of an acute infection in the nasopharynx by way of the tuba auditiva. It may be carried to the tympanum by way of the lymphatics or blood supply, or it may enter from the external meatus as the result of a traumatic rupture of the drum-membrane. It is a frequent complication of acute infectious disease, especially scarlet fever and measles.

The process produces a marked swelling of the mucous membrane of the tympanum, which in most cases involves the tube as well as the attic, aditus and antrum, and not infrequently the pneumatic spaces of the mastoid process. In a short time after the onset, the middle ear chambers are filled with a purulent exudate, which in the beginning is more or less serous and often hemorrhagic. Eventually the pus breaks through the drum-membrane and discharges into the external meatus.

The **symptoms** are severe persistent earache, a more or less marked elevation of temperature, especially in children, and a decided defect in the hearing. The pain is likely to be continuous, gradually increasing in intensity until the drum-membrane ruptures; but it may be absent entirely or present only for the first few hours after the onset. As a rule, the pain is continuous and not intermittent, as is often the case in the serous form of otitis media. The elevation of temperature in children is not infrequently 104 to 105°F. before the ear begins to discharge. A sudden drop to normal or subnormal when other symptoms persist is always an ominous sign in children, frequently heralding the development of an intracranial complication.

The defect in hearing is quite marked as the result of obstruction in the sound-conducting mechanism. It is not uncommon, however, to discover a defect at the upper end of the tone scale, indicating a degree of nerve deafness associated with the defect due to middle ear obstruction.

The appearance of the drum-membrane is very characteristic. There is a congestion and thickening which obliterates the normal landmarks, especially the cone of light and the line of the manubrium. The upper posterior quadrant is frequently bulging into the canal from the pressure of the secretion in the tympanum. After the perforation has taken place, the meatus is filled with pus, which can usually be seen to pulsate. An inspection of the drum-membrane, even before the perforation has taken place, is not infrequently obscured by desquamation of epithelium, which is removed with considerable difficulty, owing to the extremely sensitive condition of the membrane.

Acute purulent otitis media usually runs its course in uncomplicated cases in from two to three weeks. The initial stage before the rupture of the drum-membrane lasts anywhere from a couple of hours to several weeks. As a rule the spontaneous perforation takes place within two or three days. With the rupture of the membrane the pain suddenly disappears, and the temperature subsides almost to normal. The stage of active discharge varies from a few days to a few weeks in the uncomplicated cases. At the onset the discharge is usually quite profuse, rather thin and not infrequently blood-tinged. After a few days it becomes more distinctly purulent and, by the end of the first week, distinctly mucous in character.

The **diagnosis** must be made in the beginning from the acute serous oititis media. As pointed out above, this is by no means always possible. As a matter of fact, between the milder cases of acute serous otitis media and the more severe cases of acute suppurative otitis media there is no difficulty in making a diagnosis, but all grades of severity present themselves so that there is in reality no sharp distinction to be drawn between the strictly serous and the strictly purulent cases. The most that can be said is that some cases are more serous than purulent, while others are more purulent than serous. It is a mistake to attempt to draw the distinction between these two types too sharply, especially when it comes to the question whether one should advise paracentesis.

One should keep in mind the fact that the symptom of earache is by no means restricted to cases of acute otitis media. It is often a referred pain from the teeth, in children from cutting teeth and in adults from carious or embedded molars. It may be referred from acute inflammation of the faucial or pharyngeal tonsils. Moreover, the presence of discharge in the external meatus may be due to other causes than from a suppurative otitis media. The meatus is often filled with secretion in cases of diffuse otitis externa or in cases of furunculosis of the meatus. Both of these conditions are not infrequently complications of a purulent discharge from the middle ear. The diagnosis of an otitis media in the presence of a well-developed otitis externa is not always easy.

The **treatment** of acute purulent otitis media may in the first stages be symptomatic. To quiet the pain 5 per cent. solution of carbol-glycerine, warmed and dropped into the ear, is perhaps the most effective remedy. To this may be added the external application of heat, as recommended for the serous form of otitis media. As soon as the severity of the symptoms warrant the probable diagnosis of a beginning purulent rather than a serous process or when the inspection of the drum-membrane indicates this diagnosis, one should proceed at once with a paracentesis.

The opening of the drum-membrane is carried out by making as long an incision as possible close along the posterior margin of the manubrium, and extending it toward the lower margin of the membrane. In cases where a sagging of the upper posterior quadrant exists, the opening should be made through the bulging portion. The method of making an extensive incision, beginning in the upper posterior quadrant and extending well out along the upper wall of the external meatus, is not to be recommended. In the first place, the only part of the incision which accomplishes any result is that through drum-membrane; and in the second place, in making such an incision there is danger of injuring the articulation of the incus with the stapes. The opening of the drum-membrane should be carried out under proper antiseptic precautions. The operation is done very quickly and may be accomplished without the assistance of anesthesia. On the other hand it should be remembered that the operation is often intensely painful. For this reason one may use a local anesthesia to advantage. For this purpose various preparations have been used, such as 10 per cent. novocain, adrenalin solution, or a 5 per cent. cocain-adrenalin solution, warmed and dropped in the ear and allowed to remain for a few minutes. It is difficult to get a satisfactory local anesthesia because of the failure of the epidermis covering the outer surface of the membrane to take up the solution, except in cases where this layer is macerated as a result of the inflammatory reaction. The most effective way of securing a satisfactory local anesthesia of the drum-membrane is by mixing a few crystals of cocain, menthol and carbolic acid in equal parts. A small pledget of cotton on a suitable cotton carrier is dipped in this preparation and then applied carefully to the part of the membrane to be incised. Only a small drop of this preparation is necessary. In children over three or four years, nitrous-oxide anesthesia is often advisable.

After the drum-membrane has been opened, the after treatment consists of placing narrow gauze strips in the external meatus to take up the secretion, or the same result may be accomplished by pledgets of cotton twisted out to a point, which act as a wick when inserted into the canal. These should be removed as often as they become saturated. Heat should be applied from time to time in the form of a hot-water bag or an electric pad. Not only is this the best means of quieting a persisting earache, but it also has a distinct therapeutic value by facilitating the discharge from the tympanum. Cleansing the ear by douching is not necessary in the early stages after the paracentesis and is to be used later only in cases where a thick purulent discharge cannot be removed readily by other methods. Where the secretion becomes thick and shows a tendency to crust, the cleansing may be facilitated by instillation of peroxide into the canal.

Acute purulent otitis media in infancy is a very frequent disease and presents many peculiarities not met with later. The cause for the extreme frequency of middle ear infection in infancy is due in part to the fact that the middle ear chambers in the newborn are filled with a gelatinous thickening of the lining membrane, which in the course of degeneration and atrophy renders these chambers much less resistant to infection, whether from extension from the nasopharynx by way of the Eustachian tube or through the blood stream or lymphatics. The Eustachian tube in the infant is much shorter and more open than later in life, thus facilitating the entrance into the tympanum of secretion from the nasopharynx. The frequency of stomach disorders associated with vomiting also leads to frequent infection of the middle ear by the entrance of infectious material through the tube. To these causes should be added the inability of the young child to keep the nasopharynx free from secretion, which, may readily find its way up through the tube into the tympanum because of the position of the child in bed. Badly nourished infants, especially those with hereditary constitutional diseases, children suffering from tuberculosis, syphilis, rickets, or scrofulous trouble are peculiarly susceptible to acute suppuration of the middle ear.

The symptoms of this trouble are in many respects quite peculiar in infancy. There is a marked tendency for the disorder to produce no other symptoms than fever. This is no doubt, in part only apparent as it is only after the third or fourth month that the child will indicate ear trouble by carrying the hand to the ear or side of the head or even show discomfort when the auricle is manipulated. For this reason ear examination should be part of the routine when fever develops in an infant, especially when it is not readily accounted for otherwise. The fever from an acute otitis media is unusually high in these cases. An elevation of 104 or 105°F. is not uncommon. The onset is often associated with a chill or with vomiting. Marked nervous symptoms are often present, such as convulsions or symptoms characteristic of a meningitis, such as retraction of the head, stupor or sudden restlessness. These symptoms disappear quickly after the drainage through the drum-membrane has been established. The condition has been termed *meningismus*. When the meningeal symptoms do not quickly subside after a paracentesis, the beginning of a true meningitis should be suspected.

Examination of the drum-membrane in infancy presents unusual difficulties. The canal is so small that the ordinary ear speculum cannot be used. The freeing of the meatus from obstructions, such as cerumen or desquamated masses of epithelium, is frequently a difficult procedure, requiring skill as well as patience. When this cannot be accomplished rather readily by means of small pledgets of cotton on a suitable cotton carrier, or by small blunt hooks made especially for the purpose, one may instill peroxide in the ear and after a few minutes syringe out the canal with warm water. It must be remembered when interpreting the findings on the drum-membrane that manipulations from cleansing the canal often produce more or less congestion of the drum-membrane and that even the infant's crying will produce a temporary congestion. Finally, one must remember that the drum-membrane at this period is much thicker and less pliable than later in life and that the color from secretion in the tympanum is never so distinct. The characteristic bulging of the membrane is more rarely observed than after the child is two years old. The course of otitis media of infancy is often peculiar. A spontaneous perforation of the membrane is prone to be slow in forming, often not taking place for several weeks, during which period there may be no symptom other than the elevation of temperature. This is likely to be continuous with little tendency to fluctuations. When there is a sudden drop to subnormal, one should be suspicious of an intracranial complication. The drop in temperature after the rupture of the membrane is likely to be much less marked than in older children. Indeed, it is not uncommon for a rather high temperature to persist over several weeks in cases which develop no complication and which eventually go on to a complete recovery.

The period of discharge is likely to be very much prolonged no doubt due in many cases to an unusual tendency for the development of granulations, which tend to retard the free escape of pus. Another cause is the fact that middle ear infection so frequently develops in badly nourished infants or in those suffering from some general disease.

No mastoid process exists at this period, but a subperiosteal abscess over the site of the mastoid frequently develops in these cases. The condition develops with unusual rapidity, the complication arising from an extension from the antrum, the outer wall of which is very thin, quite porous, through which the more or less patulent petrosquamosal suture passes. For these anatomical reasons it is not so uncommon to observe changes in the soft structures back of the ear, which disappear spontaneously after the ear has begun to discharge, exactly as the symptoms of meningismus disappear after the paracentesis.

The unusual course taken by many cases of acute otitis media in infancy, the absence of pain, the late development of the perforation in the membrana tympani, the formation of exuberant granulations in the fundus of the canal, tend to make one suspicious of a tubercular process, as these symptoms are more or less characteristic of tubercular disease of the middle ear later in life. Indeed, it is not uncommon for tubercular disease of the middle ear to develop before other evidences of this condition have been detected. On the other hand, one is not justified in making a diagnosis of tubercular disease of the middle ear from the above symptoms.

In the treatment of acute otitis media in infants, the first thing to emphasize is its early recognition and relief by a timely paracentesis. When the incision of the drum-membrane is followed by a rather thin, sanguinous fluid, one can feel satisfied that the opening has been made in time, that is, before a serious destruction of tissue in the tympanum has developed. On the other hand, when the paracentesis is followed by the filling of the meatus with a thick purulent discharge, it indicates that the most favorable period for the paracentesis has already passed. The second point in the treatment of these cases is the timely removal of such exuberant granulations as tend to prevent the free escape of pus from the tympanum. This condition not only increases the risk of a complication, either an intracranial involvement or a subperiosteal abscess over the mastoid region, but is prone to lead to a chronic middle ear suppuration, which may later require operative treatment.

In the treatment of the ear after the discharge has begun, great care should be exercised in keeping the meatus cleansed. Owing to the sensitive skin, a troublesome dermatitis in the form of a diffuse eczema is very likely to develop. It is well to keep the auricle well protected during the period of discharge by frequent applications of olive oil or vaseline. When there exists a marked enlargement of the faucial and pharyngeal tonsils, these should be removed after the subsidence of the otitis media. In some cases the presence of this condition in the pharynx tends to cause the ear trouble to become chronic, and it may be necessary to remove them before the middle ear disease will heal.

Acute Suppurative Mastoiditis.—Acute inflammation of the mucous membrane lining the pneumatic spaces of the mastoid process is a frequent complication of acute suppurative otitis media. Where the opportunity has presented itself for making a post-mortem examination a few days after the onset of otitis media, the frequent occurrence of acute mastoiditis in cases where no clinical symptoms suggested its presence has been demonstrated. The frequency with which the pneumatic spaces are involved in acute otitis media is not surprising in view of the free communications between the antrum and the pneumatic cells of the mastoid, and the fact that the antrum itself is really a part of the tympanum, with which it is connected by a large passage, the aditus ad antrum. Because of this relation, the antrum partakes of practically every severe inflammatory reaction which invades the tympanum proper.

Most cases of acute mastoiditis, like most cases of acute otitis media, go on to a spontaneous recovery. In other cases the accumulation of pus in the mastoid cells leads to a melting down of the bony partitions between these cells and the formation of a smaller or larger mastoid abscess. Even in cases where the mastoid process has remained diploetic, small scattered abscesses may develop which form by confluence a single large abscess cavity. The spontaneous healing of an abscess cavity is possible either by the rupture of the abscess into the antrum, allowing the free escape of pus through the perforation in the drum-membrane, or by a perforation through the cortex of the mastoid on the outer surface of the process or into the external meatus. In other cases the perforation may be on the inner aspect of the mastoid tip, leading to the formation of a deep-seated abscess in the neck. The inner table of the process may be perforated and lead to an intracranial complication.

Mastoiditis is usually secondary to an acute otitis media, the result of direct extension by continuity from the disease of the tympanum and antrum. In such cases a free communication exists, at least at the onset, between the inflamed mastoid cells and the tympanum and antrum. Later this communication may cease to exist due to swelling of the mucous membrane and the formation of granulations closing the communicating passage. This obstruction is usually between the mastoid cells and the antrum and not, as is sometimes supposed, in the passage from the antrum to the tympanum, the aditus ad antrum. In other cases development of the mastoid infecton is by metastasis, where no communication exists from the onset between the disease in the tympanum and that in the mastoid process. In such cases a communication may be later established by the perforation of the abscess into the antrum.

Mastoiditis occasionally develops primarily, that is, without a preexiting inflammation in the tympanum. In these cases the infection may enter the mastoid from the nasopharynx without producing a reaction in the tube or tympanum, or it may be the result of an hematogenous infection. In rare cases the primary mastoiditis is the result of external injury to the mastoid process.

The typical mastoid abscess begins to produce its characteristic symptoms about the second or third week after the onset of the otitis media. It is not uncommon for symptoms of mastoiditis, more or less pronounced, to develop at the very onset of the otitis media before the drainage from the tympanum has been established. In such cases these symptoms promptly disappear, as a rule, with the timely opening of the drum-membrane, but when the opening is delayed, the mastoiditis is likely to proceed to a softening of the bone and the formation of an abscess cavity. In still other cases the evidences of mastoiditis do not present themselves until after the reaction in the tympanum has subsided and the perforation in the drum-membrane has closed. Acute mastoiditis occurs also as a complication of a chronic otitis media, where it is the result usually of an acute exacerbation in cases where a cholesteatoma formation exists.

The **symptoms** in a typical case of mastoiditis can hardly be mistaken. Most conspicuous are the changes in the soft structures over the mastoid, itself. These alterations are best observed by standing behind the patient, who sits with back to the light and head tilted slightly forward. This permits of a ready comparison between the two sides. The first evidence of changes in the soft structures will be an obliteration of the crease which usually marks the separation of the auricle from the mastoid. In exceptional cases, only, is this crease normally absent. Here a comparison with the normal side will readily disclose such a condition. Pressure with the finger tip over the surface of the affected mastoid will demonstrate the existence of edema even in cases where very little thickening of the soft tissue can be discovered by inspection. In advanced cases swelling over the mastoid becomes very much in evidence, displacing the auricle forward and downward in a most characteristic manner. Such a displacement may be seen by viewing the patient from in front though not so well as from behind.

In cases of mastoiditis where alteration in the soft structures has begun, the process is found to be distinctly more sensitive to pressure than normal side. This sensitiveness to pressure may be detected in many cases where no alterations in the soft structures can be seen. In other cases, especially in adults where the outer table of the mastoid is thick and hard, no changes in the soft structures can be discovered either by inspection or by palpation, when the whole process may be found occupied by a large abscess cavity.

Examination of the external meatus frequently discloses characteristic evidences of a mastoiditis even in cases where the region back of the ear appears quite normal. This consists of a characteristic sinking of the upper posterior wall of the bony meatus. Such a depression has exactly the same significance as a swelling over the surface of the process. The position of the antrum is above the upper posterior wall of the external meatus, just external to the drum-membrane. Moreover, with the development of the mastoid process and its pneumatization, a segment of the upper posterior part of the bony meatus is formed from this process. An acute periostitis over this part of the bony meatus may develop from inflammatory disease of the mastoid cells.

Examination of the discharge often gives important evidence of an existing mastoid abscess. In the typical uncomplicated cases of acute otitis media the discharge at the onset is thin and rather serosanguinous in character. It increases rapidly in amount during the first two days, when it begins to become more distinctly purulent. By the end of the first week the amount of the discharge has already begun to diminish and it takes on a more mucous character. When a mastoid abscess is forming the discharge becomes more and more purulent as time goes on, and the amount shows no inclination to decrease. When such a condition persists for a period of four weeks, the diagnosis of a mastoid abscess can be made, even when other symptoms are entirely absent. On the other hand one should not lose sight of the fact that a sudden diminution of the discharge from the ear or its complete cessation is often an evidence that a mastoid abscess has broken through its bony wall. When the perforation is external, evidence can be discovered over the surface of the process or deep in the neck beneath the tip. When the rupture has been internal, symptoms of an intracranial complication soon begin to appear.

The bacteriologic examination of the discharge found in the external meatus gives very little reliable information, owing to contamination of the discharge after it escapes into the canal. Most of the cases which go to a breaking down of the bone are the result of a streptococcus infection, as can be determined by examination of the pus found in the abscess at the time of the operation.

The general symptoms in uncomplicated cases of acute mastoid abscess are not especially significant. In adults there is usually only a slight elevation of temperature, not over 99 or 100°F., or it may be absent most of the time in exceptional cases. In children an elevation of 102 to 103°F. is not exceptional. It is of the continuous type. The fluctuations that occur can be explained as the result of obstruction to the escape of pus. The general condition of the patient depends in part on the degree of temperature but is even more dependent on the presence or absence of the symptom of pain. A mastoiditis causing pain produces a marked effect on the general condition of the patient, whereas large sub-periosteal abscesses, pushing the auricle away from the side of the head, are not infrequently observed in children who are free from pain and where the general appearance of the child shows little indication of illness. Little importance can be attached to the result of transillumination other than confirmatory evidence that the mastoid cells are filled with pus. The skiagraph, on the other hand, will not infrequently show that an actual breaking down of the bone has taken place with the formation of an abscess cavity. It is especially valuable in those cases where other evidences of this condition are absent.

Differential diagnosis has to do chiefly with the reaction over the mastoid which may develop in cases of deep-seated furunculosis in the external meatus. The edema and swelling of a furuncle may even displace the auricle, but this displacement is more upwards rather than a downward displacement characteristic of a mastoid sub-periosteal abscess. In furunculosis the edema is likely to extend beyond the confines of the mastoid, involving even the soft tissues about the eye. There is, moreover, an absence of spontaneous pain over the process, or of pain elicited by deep pressure, which is so characteristic of mastoiditis. An examination of the external meatus will disclose the presence of the furuncle, and, when it is possible to introduce a small speculum, both the appearance of the drum-membrane and the fact that there is practically a normal hearing will demonstrate the absence of an otitis media. In those cases where the otitis externa is a complication of an existing purulent otitis media, the diagnosis may not be so clear and may require several days' careful observation. There is another condition which may be confused with a mastoiditis. This is a swelling with even ultimate breaking down of the lymph gland located over the mastoid. This condition may be a complication of an otitis externa, when the differential diagnosis is made, much as in the case of furunculosis.

The **treatment** of mastoiditis may be a conservative or an operative procedure. The conservative treatment aims first of all to maintain free discharge from the perforation in the drum-membrane, combined with rest in bed and the application of heat, especially in the form of moist dressings.

The indications for operative treatment do not depend entirely upon the local findings. One should not lose sight of the fact that many cases with well-marked evidence of a mastoidits, even with the characteristic swelling and edema over the process, do not require operation, and that on the other hand cases urgently requiring a mastoid operation frequently occur, especially in adults, where the local symptoms, such as changes in the soft structures over the process, are entirely absent. The importance to be attached to certain symptoms depends largely on the time when these symptoms occur, as well as on their duration. For example: Well-marked symptoms of mastoiditis appearing early in the course of an acute otitis media before the drainage from the tympanum has been established have not the same significance as do symptoms much less marked which develop several weeks after the onset of the discharge. The mastoid symptoms which are present at the onset of otitis media disappear, as a rule, very quickly after the ear has begun to discharge. On the other hand, when these symptoms appear after the ear has been discharging for a couple of weeks, they usually signify a softening within the mastoid process which requires operative treatment. The prolongation of mastoid symptoms for a week after drainage has been established also indicated a process requiring surgical interference. In this connection we would point out the harmful effects of delay in establishing drainage from the tympanum. The longer the otitis media exists before the opening of the membrana tympani is accomplished, the more probable is it that alterations in the mastoid process requiring operative treatment have taken place. The spontaneous rupture of the drum-membrane is not infrequently delayed a week or more in cases, especially where pain has been present only during the early stage. It is highly important that in such cases the condition should be recognized and a timely paracentesis carried out.

The complete absence of symptoms over the mastoid does not exclude the possibility of a mastoid abscess, especially in adults where the outer shell of the process is frequently quite thick and hard. Here the continuation of pain limited to the same side and frequently referred to the temporal region is often present. When a profuse purulent discharge persists with no evidence of abatement for a period of four weeks after the opening of the membrane, the existence of an abscess is very probable, especially in adults. The skiagraph will usually confirm the diagnosis by showing the exact size and location of the area of softening in the bone. In young children the existence of a mastoiditis is not likely to remain obscured for the reason that the outer shell of the process is still quite porous and the more or less patulent petrosquamosal suture also readily permits of extension of the infection to the periosteum. In children under six or eight years of age the mastoid abscess is with very few exceptions in free communication with the antrum, whereas in adults an abscess which does not communicate with the antrum is not uncommon.

The operative treatment for an acute mastoid abscess is not the same for all cases. When an abscess is found at a distance from the antrum with no evidence that it connects with this chamber the removal of the outer shell of the process and the draining of the abscess, taking care to remove all softened bone, will suffice to bring about a speedy cure. On the other hand, when there exists a communication with the antrum, which condition can usually be determined by the evidence of softened bone in the region of this chamber, all such diseased bone should be carefully curetted away, and a free opening with the antrum established. The cavity, itself, of the antrum should be interfered with as little as possible because of the risk of dislocating the incus. In young infants no mastoid process exists, and any involvement of the soft structures over this region means an extension from the antrum. This may take place with the formation of a subperiosteal abscess through direct extension by way of the petrosquamosal suture without any trace of softening in the bone. It is in these cases, but in these alone, where Wilde's incision, the old method of relieving a manifest mastoiditis by making an extensive incision through the periosteum over the mastoid, may be employed with good results.

The operation is ended by closing the skin incision both above and below, leaving only sufficient opening near the center to permit the introduction of a gauze packing. This requires removal, in the ordinary case, only after six days. After that the gauze packing should be renewed every day or every second day. The time required for the wound to heal is from three to six weeks, except in cases where a debilitated general condition or some constitutional disease, such as tuberculosis, syphilis or diabetes, interferes with the healing process. Where the healing is retarded by the development of exuberant granulations, applications of a preparation of scarlet red may be employed as long as the opening into the antrum persists. After that, silver nitrate in solution or by the application of the stick is the best means for keeping them reduced.

Chronic Suppurative Otitis Media.—Chronic suppuration of the middle ear is a disease which owes its origin in the great majority of cases to middle ear infection acquired in early childhood. It is characterized by a thickening of the mucous membrane lining the tympanum, often by the formation of granulations and polyps, a more or less extensive destruction of the drum-membrane and a purulent discharge. Not infrequently the process is not restricted to changes in the mucous membrane lining the middle ear chambers but involves the underlying bone, either in the form of caries or as the result of a cholesteatoma formation.

The chronic process takes its origin from an acute otitis media. The condition which leads to the persistence of the inflammation and the development of the chronic process is not the same in all cases. Foremost among these causes is the retention of discharge, usually as the result of the development during the acute stages of obstructing granulations or of polyps. In other cases such obstructions are caused by the presence of normal mucous membrane folds connecting the ossicles with each other and with the walls of the tympanum, especially where these folds have been thickened as the result of previously existing chronic adhesive middle ear catarrh. Another common cause for the development of chronic otorrhea is to be found in the character of the changes produced during the acute middle ear reaction from which the chronic process takes its origin. It is not uncommon for the more severe acute processes to produce a softening in the bone in the immediate vicinity of the middle ear chambers. This may be in the walls of the tympanum, especially in the recessus epitympanicus or the recessus hypotympanicus. More frequently this softening of the bone is located in the walls of the antrum or in the bony partitions separating the mastoid cells, as discussed in the section on "Acute Suppurative Otitis Media." When such caries of the bone, whether it be in the mastoid or elsewhere, does not receive surgical treatment, which is a frequent enough omission, the process is certain to become a chronic one, constituting the basis for a chronic middle ear suppuration.

It is probable that chronic catarrhal conditions of the nasopharynx, especially such as are associated with enlargement of the tonsils and adenoids not infrequently act as a cause for chronic middle ear suppuration by prolonging any inflammatory middle ear process.

A weakened general condition of the patient, whether the result of malnutrition, anemia or such conditions as syphilis or tuberculosis, may prolong the healing of the acute middle ear inflammation until secondary changes in the mucous membrane of the tympanum develop which prevent the process of healing.

It is a well-known fact that a suppurative middle ear process restricted to the attic with a perforation in Shrapnell's membrane rarely, if ever, runs an acute course. The chronic character of the disease is apparently due primarily to faulty drainage resulting from the mucous membrane folds between the ossicles and the attic walls, which leads eventually to development of carious processes.

In a discussion of the **symptoms** and **treatment** of chronic suppurative otitis media, we would emphasize the occurrence of two distinct types of processes, the one where the inflammatory changes are restricted to the mucous membrane lining the middle ear chambers, the other where these changes are associated with a bone invading process. The former are by far the more frequent and constitute, on the whole, relatively harmless affairs, from which serious intracranial complications rarely, if ever, develop. The latter are rather the exceptional cases of chronic middle ear suppuration but are the cases which constitute a distinct menace to the individual in that they lead not infrequently to serious, often fatal, intracranial complications. The simple cases of chronic otorrhea call for local conservative treatment, which should not be replaced by radical operative treatment even when it is not possible to entirely check the chronic discharge by conservative treatment. On the other hand, conservative treatment will not suffice in cases where the disease has extended to the temporal bone, and because of the danger of serious complications, radical surgical treatment should be employed.

Simple Chronic Middle Ear Suppuration.—As regards the simple cases of middle ear suppuration, those in which the disease is restricted to involvement of the mucous membrane, the symptoms consist of a discharge associated with a more or less marked depression of the hearing function. The discharge may be quite profuse and is usually more or less mucous in character, especially when there is an associated acute inflammation in the nasopharynx. It is not foul smelling except in cases where the local cleansing has been neglected, and then only moderately so. The discharge may be somewhat sanguinous when the condition is complicated by the development of granulations or polyp formations.

The perforation in the drum-membrane occurs under a variety of forms, but withal presents certain well-recognized characteristics. The perforation may be small but is more often quite extensive, including most of the pars tensa. It is always restricted to the pars tensa and is central in character for the margin is not involved even in the cases where there is practically complete loss of the membranes.

The defect in the hearing shows the characteristic reactions of obstrusive middle ear deafness. The degree of the defect has very little to do with the size of the perforation in the drum-membrane. In many cases where there exists a practically complete destruction of this membrane the hearing is but slightly depressed. The more severe loss of hearing is usually due to fibrous thickenings around the labyrinth windows. The stapes constitutes the key to the sound conducting mechanism and so long as the movements of this ossicle are not impaired, very little loss of hearing from the middle ear disease is likely to result. In some cases the defect in hearing due to obstruction in the sound conduction is complicated by a more or less extensive degeneration in the basal coil of the cochlea, as evidenced by a more or less extensive depression of the upper tone limit. A secondary labyrinth degeneration is especially likely to be discovered in those cases where an annoying tinnitus persists. These secondary changes in the internal ear are prone to develop in long-standing cases of middle ear suppuration and constitute one of the main causes for an increase in deafness, which so frequently appears about middle life or later in cases where the middle ear suppuration, with a moderate defect in the hearing, has existed since childhood.

Pain is rarely a symptom of simple cases of chronic otorrhea except as it represents an acute exacerbation from a fresh invasion, which so frequently follows an acute pharyngitis. Occasionally pain may result from a more serious obstruction of the escape of pus, especially where polyp formations exist.

The diagnosis of the simple middle ear processes from those in which the bone is involved is not difficult as a rule, but may require careful observation over several days or weeks in doubtful cases. The diagnosis of a simple process is based on the symptoms already described, especially the character of the discharge, the type of the perforation and the absence of pain.

The **treatment** is always a conservative one and consists, in the first place, of the correction of any existing obstruction to the escape of pus, such as exuberant granulations or polyp formations. The former are most effectively handled by applications of chromic acid, which for this purpose is melted into a small bead on the end of a probe. Immediately after the application one must be prepared to irrigate the ear, as the melted acid tends to run down quickly through the Eustachian tube. In cases where the ear is very sensitive, local anesthesia may be employed as described under "Paracentesis." The polyps are best removed by means of a fine wire snare. Where the base of the polyp is cut through by the wire, it may require cauterizing with chromic acid, which is best carried out a few days after the removal of the polyp.

The proper cleansing of the discharge from the ear is an important part of the conservative treatment. This may be done by using small pledgets of cotton on suitable carriers, but often it is necessary to use irrigation, especially to remove more or less inspissated masses of secretion. For this purpose warm sterile water may be used to which peroxide may be added.

The best preparation for the patient, himself, to use is a saturated solution of boric acid in 95 per cent. alcohol. This should be poured into the ear warm and allowed to remain for several minutes. The first applications are likely to cause more or less burning, when the solution may be diluted with water. This preparation is used after the ear has been cleansed either by irrigation where the discharge is very profuse or by means of the cotton swab. It is important to remember that continued irrigation not infrequently prevents the cessation of the discharge, so that one should resort as soon as possible to the dry method of treatment, cleansing by means of dry cotton swabs followed by insufflation of a small amount of finely powdered boric acid.

Under this conservative treatment many of the cases of chronic otorrhea which may have persisted from childhood into middle life may in a short time be brought to a permanent termination. In other cases the discharge is prone to start afresh with each head cold. Even in those cases where persistent local treatment fails to end the middle ear disease, one is not justified in resorting to radical surgical treatment. In the first place, this form of middle ear trouble is not a dangerous process, and, in the second place, the radical operation is likely to increase the defect in the hearing by further fixation of the stapes from dense scar formations. The radical mastoid operation may not end the discharge, which not so infrequently persists because of a focus of infection in the tube or tubal cells, which the operation has failed to eradicate. The persistence of discharge from the tube in those cases requiring radical operative treatment is not an objection to the operation since by this procedure the dangerous focus in the antrum or the mastoid, for which the operation is undertaken, has been eradicated.

A word should be added to this discussion of conservative treatment for chronic otorrhea on the closure of persisting perforations in the membrana tympani and on the use of artificial drum-membranes. Because a persisting perforation in the drum-membrane predisposes to recurring acute exacerbations and because the closure of the perforation may lead to improvement in the hearing, one is sometimes justified in making an effort to close such openings. As a rule, this is not likely to be successful except where the perforation is rather small. The closure may be accomplished by carefully cauterizing the edges of the opening with trichloracetic acid. This, of course, cannot be carried out except in cases where the discharge has been completely checked. Very often the application of the acid starts the discharge afresh. Further treatment can only be carried out after this reaction has subsided. It is evident that such efforts are permissible only for cases where the labyrinth is not involved. The use of artificial drum-membranes has a rather limited application. The term "artificial ear-drum" is a favorite one for the charlatan, as it conveys the impression that deafness is due to disease of the drum-membrane and that an artificial membrane will restore the lost function. It is sold by these quack vendors for all cases of deafness, to people with normal drum-membranes as well as to those whose drum-membranes have been destroyed. The facts about the use of the several devices which go under the name of artificial ear-drums are that in some cases of chronic suppurative otitis media with a more or less extensive destruction of the drum-membrane anything which is placed against the stapes may increase its ability to take up sound impulses and transmit them to the fluid in the labyrinth. Various substances have been employed for this purpose. A small pledget of cotton moistened with vaseline accomplishes a favorable result as often as any device. The same result can sometimes be obtained by a droplet of oil or by insufflation of dry powder. A small pliable piece of rubber, to which a thread is attached, carried into the ear by a suitable carrier, is on the whole the most useful of such devices. The rubber should be moistened with vaseline before applying. The patient usually acquires the skill to place these in his own ear to best advantage. Of course the artificial membrane acts as a foreign body and tends to continue middle ear discharge. The only cases where such devices are applicable are those with a more or less marked defect for the voice involving both ears.

Chronic Suppurative Otitis Media with Bone Involvement.—The cases of chronic suppurative otitis media in which an involvement of the surrounding bone has taken place are much less common than the simple form of otorrhea where the disease is limited to an involvement of the mucous membrane. The extension of the inflammatory process to the bone, as found in these cases of chronic suppuration, is brought about in several ways. In long-standing cases of chronic suppuration, where the disease has been prolonged through impaired drainage, this inflammatory process may gradually extend to and involve the underlying bone. Here, as a rule, a condition of caries develops, which in some cases remains circumscribed to a small area, and may get well under local conservative treatment or even spontaneously when it is confined to parts of the tympanum. In other cases a more or less extensive sequestration of bone takes place. Such cases naturally cannot heal until the sequestrum has been removed. This usually requires surgical treatment, but a spontaneous extrusion of the sequestrum also takes place.

In other cases the involvement of the bone has its origin during the violent reaction associated with the acute stage at the onset of the otitis media, and this involvement of the bone, whether it be in the tympanum, the attic or the mastoid, is the factor in the acute otitis media which retards the healing and determines the chronic persistence of the middle ear process. Here, again, we have the two forms of bone disease, a process of caries, which is the more frequent, and that of sequestration. It is probable that this method of bone involvement is the more usual one, especially since long continued observation of cases of simple chronic suppuration rarely discovers any evidence pointing to a late involvement of the underlying bone, even in those cases where local treatment is practically neglected over a long period.

There is still another way by which involvement of bone takes place in chronic middle ear suppuration: That is, by the development in the middle ear of a cholesteatoma, usually in the recessus epitympanicus or antrum. This formation, by rapid proliferation of its peripheral layers, fills the cavity and by pressure on the surrounding walls produces a gradual absorption of the bone.

Hand in hand with the development of caries or sequestration, as well as in cases of cholesteatoma, a process of sclerosis in the surrounding bone takes place, an osteosclerosis, nature's method for checking the process of the bone invasion.

In true osteitis with caries or sequestration the demarcation between the diseased and normal bone is marked by a rough irregular surface, whereas in cholesteatoma there is a smooth glistening surface with ivory-like hardening of the bony walls.

The **symptoms** produced by the bone invading form of chronic suppurative otitis media are quite characteristic as a rule and serve to differentiate such cases rather sharply from simple otorrhea. First of all is the character of the perforation of the membrana tympani. Whereas in the simple form the perforation is always central, that is, with the margin undisturbed, and restricted to the pars tensa, in the bone invading forms the perforation extends to and involves the bony margin for the attachment of the membrane, with very few exceptions. Not infrequently in this type the disease extends to the pars flaccida or may be confined to the region of Shrapnell's membrane, the pars tensa escaping entirely.

Another characteristic symptom is the offensive odor to the discharge, which persists in spite of every effort at cleansing. The reason for the persistence of odor in these cases is to be found in the fact that no efforts at cleansing succeed in reaching the crevices in the bone in which decomposition is going on.

The amount of discharge is significant only in that the more rapid the bone-invading process, the more profuse will be the discharge of pus. In cases of sequestration the discharge is most profuse. Not infrequently the discharge is so slight that the patient remains entirely ignorant of its presence. When the ear is wiped with cotton in such cases, no moisture may be discovered. Nevertheless, the characteristic penetrating odor of bone disease will be found on the cotton. In other cases the discharge forms a hard black crust along the upper bony wall of the meatus just external to the upper posterior quadrant. Because of the sensitive condition of this part of the canal, the crust is removed with difficulty at times, leaving the under surface moist with pus possessing the characteristic odor.

The effect on the hearing is usually much more marked than in the simple type of suppuration due to the more extensive alterations in the tympanum. These changes consist not only of thickened scar formations covering the windows to the labyrinth, but of chalk deposits in the tissue or to true osseous growths, completely occluding the labyrinth windows and obstructing sound conduction. A more or less extensive depression of the upper tone limit is usually observed caused by secondary fibrous changes in the beginning of the basal coil of the cochlea forming the promontory. This secondary degeneration in the labyrinth may go on to the development of profound nerve deafness through extensive cochlear degenerations without being associated with any changes in the vestibular mechanism.

The symptoms produced by cholesteatoma are, with few exceptions, so characteristic that the disease can scarcely escape detection. The whitish flakes or masses of desquamated epithelium can be removed either with a blunt hook or by irrigation. The formation of a cholesteatoma requires usually the presence of a marginal perforation. The cholesteatoma is the result of an invasion of epidermis from the external canal extending into the middle ear cavities. When a sharp margin exists, such as presents itself when the perforation is central, it is not possible for this invasion to take place. For the extension of epidermis over into the middle ear it is essential that a flattened out surface present itself. Such a surface is produced by a marginal perforation extending to the bony wall. These marginal perforations are usually located in the upper posterior quadrant, but the same result is obtained when the perforation occupies the anterior part of the membrana tympani. In some cases where the handle of the hammer is adherent to the promontory, conditions are created which permit of extension of epidermis to the walls of the tympanum.

A perforation in Shrapnell's membrane is very frequently associated sooner or later with the formation of a cholesteatoma in the attic and aditus. The invasion of epidermis here is not always dependent on an involvement of the bony margin of Rivini's segment, but may take place where the opening is confined to Shrapnell's membrane, in reality a central perforation. The process of epidermization of the attic is rendered possible in such cases by the fact that the flaccid membrane is often found adherent to the neck of the malleus. A rupture of this delicate membrane, which apparently may result from the inflation of the ear in the act of blowing the nose, opens the way for the invasion of epidermis into the attic. Later such cases may become infected, setting up secondary chronic suppuration. In those cases where the bony margin is involved, the invasion of epidermis appears to be undoubtedly secondary to a chronic suppurative process just as takes place in the tympanum proper.

The diagnosis of the bone invading form of chronic middle ear suppuration from the simple form presents little difficulty, in view of the different symptoms of the two conditions. The course of the disease separates this form of middle ear suppuration most sharply from the simple type. It is the exceptional case where conservative treatment will effect a cure or where the healing takes place spontaneously. Such an outcome may take place, however, especially where the process is limited to the walls of the tympanum or where it involves only the ossicles. It is also observed in cases of attic suppuration with more or less extensive destruction of the margin of Rivini's segment. Even a cholesteatoma in the antrum may extrude itself by destroying the upper posterior wall of the bony meatus, leaving the tympanum and antrum one cavity, lined by a thin layer of epidermis quite similar to the result obtained in the most favorable radical mastoid operations.

The **treatment** of this form of chronic otorrhea in relatively few cases can be restricted to conservative local measures. In spite of every effort, in the great majority of cases the process progresses and further invades the bone. The most frequent cause for otitic intracranial complications lies in this form of middle ear infection. It is apparent, therefore, why radical surgical measures should be resorted to in order to eradicate such a dangerous focus. The conservative treatment should be restricted to the cases especially where the disease is confined to the tympanum. In all other cases radical operative treatment alone is likely to bring the disease to a termination. A contra-indication to operative treatment exists where the hearing in the opposite ear is more seriously affected so that the patient relies for his hearing on the affected ear. Even in such cases the operation has to be done where evidences of extensive erosion appear exposing the dura or the sinus. This is indicated by the symptoms of beginning intracranial complications, facial paralysis or erosion of the labyrinth capsule.

Ossiculectomy may give good results in those cases where the disease of the bone appears to be restricted to involvement of the ossicles. In all other cases the radical mastoid operation has to be carried out. This operation consists of making an opening into the antrum, removing the posterior wall of the external meatus and the outer wall of the attic, thus making the tympanum, attic, aditus and antrum one common cavity, curetting out the tubal orifice and, finally, making a plastic of the membranous external meatus so as to secure epidermization of this cavity. The incision back of the ear is closed by primary suture except for cases where an intracranial complication existed. The radical mastoid operation rarely comes into question during the period of early childhood for the reason that the chronic changes necessitating the operation are rarely apparent during this period. As a matter of fact this operation is rarely, if ever, undertaken on children under five years of age.

Complications of Suppurative Otitis Media.—There remain still to be considered the more serious complications of suppurative otitis media, including the labyrinth invasion and the intracranial complications.

Labyrinth Complications.—In this connection we restrict the discussion to the circumscribed invasion of the labyrinth, the result of a labyrinth fistula and to diffuse serous and suppurative labyrinthitis.

The circumscribed invasion of the labyrinth results from the formation of a fistula through the bony capsule, usually the result of an erosion by a cholesteatoma through the horizontal canal where this lies exposed in the floor of the aditus. The opening in the bone is closed by granulations, which for a long time prevent the diffuse invasion of the membranous labyrinth. The inflammatory process remains restricted to the immediate region of the perforation. As a rule, the only symptom of which the patient makes complaint is the occasional sensation of vertigo which is brought on by sudden movements of the head as in stooping over. By compression or rarefaction of air in the external meatus the characteristic fistula reaction can be elicited. This reaction is the result of a movement of the endolymph in the canal towards the crista on compression of the air and away from the crista on suction. This movement of the endolymph on compression produces a slow movement of the eyes in the plane of the canal, that is, in the horizontal plane, towards the opposite side, followed by a quick movement towards the same side, a horizontal nystagmus. When suction is made the opposite movements take place.

Diffuse serous as well as diffuse purulent labyrinthitis produces a depression or a complete suppression of the function of the cochlea and vestibule. From the involvement of the cochlea results a depression of hearing associated with a more or less marked tinnitus. From the involvement of the vestibule and semicircular canals results a disturbance of equilibrium consisting of vertigo associated with nystagmus, nausea, and vomiting. This disturbance results from unilateral suppression of labyrinth tonus. The tonus from the normal side, acting now without restraint of opposing impulses from the affected side, tends to draw the patient over to the affected side. At the same time the eyes are drawn over to the affected side by a rotary movement followed by a quick movement towards the normal side.

The serous form, as a rule, causes only a partial suppression of function, from which the patient may make a complete recovery, whereas the purulent form always results in a total permanent suppression of function both for the cochlea and the semicircular canals. Both forms of the diffuse labyrinthitis are complications of acute as well as chronic suppuration of the middle ear. Serious intracranial complications, such as meningitis and cerebellar abscess, may result from an extension of infection by way of the internal meatus, the aqueductus vestibuli or the aqueductus cochleæ. Because of the risk of these complications, an effort should be made to provide adequate drainage for the labyrinth by operative measures. Since these complications develop only in connection with the purulent form of labyrinthitis and because in the serous form the possibility of a return to normal always exists, the operation on the labyrinth is done only in cases of the former. The differentiation of the serous from the purulent form is by no means always possible since both may produce a complete suppression of function. The operation on the labyrinth is restricted, therefore, first of all to those cases where the suppression of function has been complete, both for the cochlea and for the semicircular canals, and of these cases only those are operated where indications already exist for an operation on the mastoid or where, in the absence of indications for a mastoid operation, symptoms arise pointing to a possible intracranial complication.

Intracranial complications of suppurative otitis media include involvement of the lateral sinus, the various forms of meningitis and brain abscess. These develop as complications of both the acute and chronic forms of suppurative otitis media.

Sinus thrombosis is one of the most frequent of these complications. This may consist of a primary thrombus of the sinus by direct extension through a diseased mastoid or as a result of extension of infection through the floor of the tympanum, first causing an involvement of the bulb of the jugular, which in young children lies close to the floor of the tympanic cavity. When the sinus thrombosis is the result of mastoid infection, in the majority of cases there is a direct extension to the wall of the sinus with the formation of a perisinus abscess. In other cases healthy bone separates the disease in the mastoid from the sinus wall, and the involvement of the sinus is by a process of metastasis.

The *symptoms* of sinus involvement are so characteristic that the diagnosis can be readily made in most cases by a single examination. The onset of the process is usually heralded by a severe chill with a sudden rise in temperature to 104 or 105°F. In a typical case this may drop as suddenly to normal or subnormal in the course of 24 hours. This phenomenon is likely to repeat itself at irregular intervals, sometimes occurring every day, in others separated by intervals of two or three days. The chill may be present only at the onset. Between the attacks the patient, in uncomplicated cases, may appear quite cheerful and show very little evidence of serious trouble. The mind is quite clear until complications involving the central nervous system later produce various nervous symptoms.

The *diagnosis* is readily made in a typical case. In other cases the absence of the typical temperature curve obscures the diagnosis. In exceptional cases the presence of a thrombosed sinus may be discovered in the course of a mastoid operation, where no characteristic symptoms suggested its presence. It is important to remember that although the sinus involvement usually develops in cases showing the clinical symptoms of mastoiditis, it may develop in cases where such symptoms are absent and occasionally occurs after an acute otitis media has subsided and the perforation in the drum membrane has closed. In this connection it is important to remember that in young children the persistence of an elevation of temperature in cases of acute otitis media which eventually make a complete spontaneous recovery is much more common than later in life. The differentiation from conditions such as pneumonia and typhoid fever must also be made.

The *course* of sinus thrombosis in the large majority of cases leads to a fatal termination through development of pyemia or of an intracranial complication, unless the process is elimininated by timely surgical treatment. It is the exceptional case that proceeds to a spontaneous recovery so that as soon as the diagnosis is assured an operation should be undertaken. This consists in the eradication of the disease in the mastoid by the simple mastoid exenteration in the cases of acute otitis media and the radical operation where the sinus disease complicates chronic middle ear suppuration. The free exposure of the sinus by removal of its bony covering is followed by incising the sinus wall and the removal of the thrombus. In the cases where the thrombus is causing complete occlusion of the sinus, the operation may simply remove part of the thrombus in order to facilitate drainage leaving both ends undisturbed. It may be necessary to ligate the jugular in the neck and resect it partially or completely. In those cases where the thrombus has broken down and the sinus is filled with pus as much as possible of the clot should be removed.

Meningitis is one of the complications most to be feared in suppurative otitis media. The extension of infection from the middle ear to the meninges is especially frequent in early childhood because of the close anatomical relations between the middle ear chambers and the middle brain fossa. The two are separated by a thin plate of bone, the tegmen, which in children is quite porous and through which passes the more or less patulent petrosquamosal suture.

In children we recognize three conditions presenting symptoms more or less characteristic of meningitis. First is the condition usually designated as meningismus. Second is diffuse serous meningitis, and third, diffuse purulent meningitis.

Meningismus occurs especially in infancy, before the end of the first or second year. The patient during the early stages of an acute otitis media, before the drum-membrane is perforated, develops symptoms quite characteristic of meningitis: High fever, stupor, retraction of the head and rigidity of the neck muscles. All of these symptoms promptly disppear after the drum-membrane has been opened and the discharge from the middle ear established.

Serous meningitis of otitic origin is usually secondary to the acute form of otitis media. It is characterized anatomically by a congestion and swelling of the meninges with increased pressure of the cerebrospinal fluid. The characteristic symptoms are the development of elevation of temperature, delirium and loss of consciousness, retraction of the head, rigidity of the neck muscles and a positive Kernig sign. On spinal puncture the cerebrospinal fluid is found to be under increased pressure. The fluid, itself, is usually clear with only a moderate increase in the cellular elements and sterile. Diffuse serous meningitis may be but the early stages of a purulent meningitis. In the uncomplicated cases there is almost always a complete recovery.

The *treatment* where the symptoms develop before the drum-membrane has opened consists in making an immediate paracentesis. Should the symptoms subside promptly after the drainage from the tympanum has been established, it is apparent that the condition has been one of meningismus. On the other hand, when the symptoms persist for 24 hours after the parcentesis, one should proceed immediately with a mastoid operation. Only in cases where a distinct discoloration of the dura exists is an incision of the dura advisable. In all other cases the subsequent treatment consists of the repeated withdrawal of the fluid by spinal puncture, which should be done every few days releasing 5 to 10 c.c. each time.

Diffuse purulent meningitis constitutes the most frequent intracranial complication from middle ear suppuration occurring during the first decade. It complicates both the acute and chronic otitis media. In the chronic cases the involvement of the meninges is by direct extension through the diseased bone to the dura, whereas in the acute form the complication is usually by metastasis, where healthy bone separates the meninges from the suppurative disease in the middle ear.

The symptoms are similar to those of diffuse serous meningitis. The fluid withdrawn by spinal puncture is turbid with increase of leukocytes. The cultures contain organisms.

In fulminating cases a fatal termination may take place within two or three days. The ordinary case terminates fatally in the course of the first week. In exceptional cases an intermittent form of meningitis has been observed where the attacks have been separated by months or even years before the fatal attack, and where at autopsy the characteristic evidence of the previous attacks can be seen. The disease is almost always fatal. The cases of meningitis which make a recovery are for the most part those of the serous form of meningitis which have been mistaken for the suppurative form. However, there have been a few cases of diffuse suppurative meningitis, where pus has been discovered on incising the dura, which have eventually recovered.

The *treatment*, especially when the process has only begun, is operative, in the effort to establish free drainage. The diseased mastoid is cleaned out and the dura incised.

Brain abscess of otitic origin may be the result of extension of infection through the tegmen, producing involvement of the tempero-sphenoidal lobe, or extension to the posterior brain cavity, producing a cerebellar abscess. The latter is likely to be complicated by either a purulent labyrinthitis or a sinus thrombosis. In many cases the abscess in the brain is surrounded by a distinct capsule. In others this is wanting and the adjacent brain substance is more or less extensively involved. In the latter the odor is most offensive.

The *symptoms* of brain abscess differ widely, depending in part on the location of the abscess but even more, as a rule, on the evidences of associated complications, such as meningitis, sinus thrombosis or labyrinthitis. During the "initial stage" the symptoms are more those resulting from circumscribed meningeal irritation, such as headache, fever and vomiting. In the second stage, the "latent period," the chief symptom is the severe headache and sense of pressure in the head. During this period the patient appears ill, develops a grayish color, and loses appetite and weight. There is rarely any elevation of temperature. During the next or "manifest stage," the symptoms characteristic of intracranial pressure are present: Slow pulse, optic neuritis, and distinct focal symptoms depending on the location of the abscess. In the "terminal stage" symptoms of collapse rapidly develop, as the result of the devlopment of a diffuse purulent meningitis or the rupture of the abscess into the ventricle.

The *treatment* is surgical. An operation for the relief of a brain abscess of otitic origin is always preceded by the simple mastoid exenteration in cases of acute otitis media or the radical operation for the chronic cases. In this way the focus of infection in the mastoid from which the brain complication has had its origin is removed. Not infrequently the course of the infection from the focus in the middle ear to the brain abscess is by direct extension and can be traced at the time of the operation. In other cases the abscess develops by metastasis through blood-vessel or lymphatic channels. Here a careful search has to be undertaken to locate the abscess. The exploration is made in the middle or posterior brain cavity, depending on whether the focal symptoms suggest a tempero-sphenoidal or a cerebellar abscess. When a tempero-sphenoidal abscess is suspected, the entire roof of the middle ear chambers should be removed. After the exposure of the dura search should be made for any discoloration indicating the route of the infection. When all evidence of this sort is wanting, one should proceed with a systematic exploration of the brain by means of a suitably large aspirating needle. Where this gives a negative result and the symptoms are sufficiently threatening, incision of the dura followed by three or four punctures of the brain substance with a scalpel may be made.

Should the symptoms of ataxia and vertigo indicate a probable cerebellar abscess, an exploration of the posterior brain fossa should be made. This may be carried out in front of the lateral sinus when the abscess is a complication of suppurative labyrinthitis. In other cases the abscess is more superficial and in more or less close proximity to the lateral sinus. The exploration in these cases is made by enlarging the mastoid incision by cutting directly backwards and entering the posterior fossa just behind the sinus.

DISEASES OF THE INTERNAL EAR

Labyrinth disease is much less common in childhood than is middle ear trouble. On the other hand, the effect on the hearing from internal ear disturbances is much more serious than from middle ear disease. One should always keep in mind the fact that all cases of profound depression of the function of hearing are cases of nerve deafness caused by internal ear disease. Even the most pronounced fixation of the sound-conducting apparatus, such as results from midde ear disturbances when unassociated with changes in the labyrinth, are capable of producing only a moderate defect in the hearing.

Involvement of the labyrinth, secondary to suppurative middle ear disease, has already been discussed. Two types of internal ear disturbances arise from middle ear trouble. One is the invasion of the labyrinth by infection in middle ear suppuration. The second type consists of secondary degenerative changes involving chiefly the beginning of the basal coil of the cochlea and producing a defect in the hearing at the upper part of the tone scale. These changes are prone to develop in all cases of long-standing deafness from obstruction in the sound-conduction. They are a frequent complication of chronic adhesive middle ear catarrh as well as middle ear obstruction the result of an exhausted middle ear suppuration. In primary fixation of the stapes caused by the condition known as otosclerosis, degenerative changes beginning in the basal coil and a defect in the hearing for the upper tones is quite common. It is these changes in the labyrinth complicating the middle ear processes which become responsible for the more profound depression of hearing so frequently observed in disease of the middle ear especially after middle life.

Extension of infection to the labyrinth in cases of meningitis is a frequent cause for the destruction of hearing in children. The extension of infection to the labyrinth takes place along the internal meatus and sets up a diffuse suppurative labyrinthitis similar to the disturbances arising from invasion of the labyrinth from suppurative otitis media. It is estimated that approximately 10 per cent. of all cases of epidemic cerebrospinal meningitis which recover are left with destroyed hearing. This condition constitutes one of the most frequent causes for total loss of hearing in children, leading to deaf-mutism.

Primary labyrinth disturbances, that is, where the trouble is not associated with disease either in the middle ear or in the brain cavity, are not at all uncommon. Such disturbances are in part due to developmental anomalies involving the labyrinth and in part are the result of primary disease of the inner ear.

Developmental anomalies in the internal ear are the cause for congenital deafness. Such anomalies are in the nature of hypoplasias of the organ of Corti as well as of the trunk of the eighth nerve. The condition is but rarely associated with developmental anomalies of the outer or middle ear. Congenital deafness is often the result of heredity, where one or both parents have been born deaf or where there is a history of congenital deafness in the family. Some of these conditions bear a close resemblance to otosclerosis, a disease in which heredity is the most important etiological factor but which, as a rule, does not become manifest before the age of puberty.

Hereditary syphilis is a frequent cause for primary disease of the labyrinth acquired in childhood. It develops, usually, towards the end of the first decade, rarely after the age of 20. It is often associated with interstitial keratitis and the notching of the upper incisors characteristic of hereditary syphilis. When the condition develops rapidly, which is the rule, there will occur symptoms of disturbed equilibrium, such as vertigo and nystagmus, as well as the disturbance of hearing. As soon as the acute stage is passed, the vertigo disappears but may return from time to time as the progress of the degeneration undergoes acute exacerbations. Where the degeneration is more insidious, it may go on to complete destruction of the function of the labyrinth without ever giving rise to the symptoms of vertigo.

Primary disease of the internal ear also develops as a complication of the infectious fevers, especially scarlet fever, measles, diphtheria, influenza and typhoid. The changes here appear in the nature of a toxic neuritis. The symptoms consist of deafness and tinnitus from the involvement of the cochlea, and disturbance of equilibrium, such as vertigo and nystagmus with nausea and vomiting, from involvement of the vestibular apparatus. The disturbances of equilibrium are transitory, lasting from a few days to a couple of weeks, and occur only in cases where there is a rapid depression of function.

An involvement of the internal ear in mumps is especially to be feared. As a rule, only one ear is involved. The trouble may be restricted either to the cochlea or to the vestibule, producing a loss of hearing or disturbance of equilibrium as the case may be. In other cases the entire labyrinth is involved, and the process may involve both ears. Clinically, the internal ear disturbances suggest a labyrinthitis of the serous type, which may be either circumscribed or diffuse. Recovery may take place after the acute stage of the mumps has subsided, but not infrequently the loss of hearing is permanent.

Primary disease of the eighth nerve frequently develops in cases where neither syphilis nor the infectious fevers have had a part. Such degenerations appearing in the first or second decade sometimes show a distinct hereditary cause. In some cases the condition appears related distinctly to otosclerosis. In other cases it seems quite probable that degeneration of the eighth nerve is the result of a neuritis caused by a focal infection, such as is found so frequently in the faucial tonsils. The involvement of the eighth nerve in these cases is quite analogous to neuritis of any peripheral nerve from foci of infection. Under these cases of labyrinth disturbance from focal infection we would include those cases which occur in connection with acute articular rheumatism.

INVOLVEMENT OF THE EAR IN ACUTE INFECTIOUS FEVERS

Attention has already been called to the frequent occurrence of middle ear inflammation complicating the infectious fevers and to the fact that primary involvement of the internal ear in the form of a toxic neuritis also develops in these cases. We wish here to emphasize some of the more striking peculiarities of the ear diseases which develop as complications of acute infectious fevers.

Scarlet fever and measles are in a class by themselves as a cause for ear complications. In both diseases middle ear infection occurs with great frequency but varies widely in different epidemics. In both scarlet fever and measles we encounter an unusually severe type of middle ear infection. This severe form is more frequent in scarlet fever, while a milder form of otitis media is more common in measles. The severe cases of otitis media are characterized by the rapid development of severe symptoms, high temperature and earache, leading to an early perforation of the membrana tympani sometimes within a few hours of the onset of symptoms. Destructive changes in the middle ear are most marked. Often within one or two weeks the drum-membrane has been largely destroyed, and the tympanum becomes filled with granulations. Infection extends rapidly to the underlying bone, and very often an exfoliation of the ossicles takes place. Disease of the antrum and of the mastoid process is quite common. Changes take place quite early in the tympanum, as well as in the antrum and mastoid, which prevent healing and lead to chronic otorrhea. It is estimated that 25 per cent. of cases of chronic otorrhea owe their origin to scarlet fever or measles.

Panotitis from the simultaneous involvement of the middle ear and labyrinth is a complication of both scarlet fever and measles. The labyrinth involvement develops in connection with the violent type of otits media in which the destruction of the membrana tympani and exfoliation of the ossicles is an early symptom. The labyrinth involvement is usually in the form of a diffuse purulent labyrinthitis, which causes the complete destruction of the function of the membranous labyrinth. In only exceptional cases is the labyrinth involvement circumscribed, leaving islands of hearing for certain tones of the scale. Such cases usually develop total deafness later. The process may be restricted to one ear, but very often both sides are involved. This form of acute labyrinthitis as a part of the panotitis rarely leads to an intracranial complication. The patient usually recovers but with a total loss of hearing in one or both ears. The suppuration in the labyrinth disappears spontaneously in most of these cases. In others the labyrinth suppuration leads to sequestration of the osseous labyrinth. The reason why sequestration of the osseous labyrinth is such an unusual occurrence may be due to the fact that the blood vessels which supply the membranous labyrinth and the endosteum rarely if ever send branches into the capsule itself so that even though the ulcerative process destroys the entire blood supply of the labyrinth, the capsule still remains nourished as it receives its blood vessels from the neighboring bone.

The treatment of otitis media complicating scarlet fever and measles requires the opening of the drum-membrane as early as possible in order to prevent those destructive changes which develop so much more rapidly when the pus is confined and under pressure. Conservative treatment suffices to bring most of the cases to a favorable termination. Mastoid involvement and intracranial complications should receive prompt attention. Operative treatment for the labyrinth suppuration in cases of panotitis is called for only in cases where an intracranial extension of the infection supervenes.

The ear complications of mumps have already been discussed under "Primary Diseases of the Internal Ear."

Diphtheria produces an involvement of the external ear in the form of a severe diffuse otitis externa, which may be secondary to an otitis media or may occur independently of a discharge from the middle ear.

Middle ear involvement by extension of the infection in the nasopharynx up through the tube is usually caused in diphtheria by other organisms than that which causes the genuine diphtheria infection. An involvement of the middle ear often develops after the acute period of the diphtheria has subsided. The middle ear process may develop without severe symptoms to direct attention to the ear and persists for some time without causing a perforation of the drum-membrane but with the development of pronounced destructive changes in the tympanum. Therefore, in cases of diphtheria with a recurrence of fever after the infection has begun to subside, it is important to make a careful examination of the ear in order to recognize any existing otitis media and supply prompt drainage by paracentesis. The occurrence of panotitis is much less frequent than in scarlet fever.

Influenza very frequently produces ear complications which vary widely in frequency and severity in different epidemics. The development of blood blisters in the external meatus or on the drum-membrane is very characteristic of influenza infection. These occur in connection with an otitis media but may occur independently of middle ear infection. A neuritis of the eighth nerve is also a sequel of influenza infection.

The symptoms of otitis media complicating influenza are not unlike those of the ordinary form of otitis media complicating a head cold. The onset is usually characterized by a severe earache, and blood blisters can be detected over the drum-membrane and the adjacent wall. These blood blisters occur in the acute catarrhal type of otitis media as well as in the suppurative cases. An involvement of the antrum and the pneumatic spaces of the mastoid is a frequent occurrence. The latter not infrequently leads to a softening of the bone, necessitating a mastoid operation.

Typhoid fever is frequently complicated by acute middle ear reaction. This is often in the form of an acute middle ear catarrh, but the suppurative form of otitis media also occurs. The middle ear reaction is sometimes complicated by a diffuse serous or even suppurative labyrinthitis. Another type of internal ear trouble is observed in connection with typhoid. This is a primary involvement of the labyrinth in the form of a toxic neuritis. In these cases the ear symptoms develop during the height of the infection. Both sides are usually involved. Severe tinnitus and marked depression of hearing are the only symptoms except when one ear alone is affected. Vertigo and nausea may result from unilateral destruction of the vestibular apparatus. After the subsidence of the fever, the ear symptoms may completely disappear with the return of hearing to normal. In other cases the degeneration of the eighth nerve progresses steadily until total permanent deafness results in the course of a few weeks.

Tuberculous disease of the ear has to do for the most part with middle ear involvement. It produces symptoms quite peculiar to this disease, which distinguishes it from other forms of otitis media. One should not lose sight of the fact that infection of the middle ear in tuberculous patients is very often only an ordinary otitis media and is not caused by tuberculous infection. Tuberculous disease of the middle ear takes place by direct extension of infection through the tube by the entrance of infected sputum, primarily involving the mucous membrane and later extending to the bone. Infection may take place through the blood stream, when it may either involve the mucous membrane primarily or begin in the bone itself.

The milder form of tuberculous infection of the middle ear is seen in cases of latent tuberculosis where the primary focus of the disease is still undetected. The process begins in apparently healthy people and does not follow an acute head cold. The first symptom is a sensation of fullness in the ear followed by a marked depression of the hearing, which is not perceptibly improved by inflation. The drum-membrane is strongly congested. The condition is the result of a marked swelling of the mucous membrane lining the tympanum. The process develops without pain. Gradually a small yellow spot appears on the membrana tympani, indicating the point where the spontaneous perforation soon takes place. This perforation usually increases rapidly in size. Not infrequently two or more perforations appear, which by confluence may eventually join to form one large opening with irregular outlines. Any acute otitis media which develops without pain and leads rapidly to a melting down of the drum-membrane should be suspected as tuberculous. In some cases the perforation remains a small pinhead or even pinpoint perforation. When such a perforation is found in a case of long-standing persistent discharge, one should suspect tuberculosis.

Not infrequently after the formation of a larger perforation in the drum-membrane the process may remain stationary or even heal.

The more severe form of tuberculous disease of the ear develops, as a rule, in cases of advanced phthisis. The process extends rapidly from the mucous membrane over into the bone and may eventually involve the internal ear in a panotitis similar to that of scarlet fever and measles. The external meatus is found filled with foul-smelling discharge and, by means of a sound, the roughened carious bone or a sequestrum can be detected. Characteristic is the relative absence of granulations in the presence of an extensive bone disease and very marked depression of the hearing or even complete nerve deafness. Paralysis of the facial nerve is not infrequent, and the lymphatics about the ear, especially in children, are likely to be swollen.

The **treatment** of the milder cases of tuberculous otitis media consists in cleansing the ear and insufflation of dry powder such as boric acid. Iodoform powder seems to be especially effective in these cases. The radical mastoid for the severer cases is undertaken only exceptionally and then in cases where the general condition of the patient is still fairly good and where there is practically no elevation of temperature. In other cases one restricts the treatment to conservative measures, local cleansing, insufflation of iodoform powder and removal of sequestra.

DEAF-MUTISM

Deaf-mutism may be congenital or acquired. By congenital deaf-mutism is meant those cases where the loss of hearing, which renders it impossible for the child to learn to speak, has developed before the age when speech is undertaken. It includes, therefore, both cases of congenital deafness and those where the hearing has been destroyed during the first year or two. Acquired deaf-mutism, on the other hand, includes those cases where the destruction of hearing has come on after the child has begun to talk and where the art of speech is lost after the destruction of hearing. It includes cases where the deafness has come on before the sixth or eighth year, seldom later.

Statistics show that the number of cases of acquired deaf-mutism is somewhat greater than of congenital cases. A great many cases develop during the first three years. Bezold has shown that of acquired deaf-mutism 52 per cent. are caused by labyrinth complications occurring during meningitis, that scarlet fever is responsible for 18 per cent., hereditary syphilis and chronic suppurative otitis media each 6 per cent. The remaining cases are caused chiefly by trauma, measles, diphtheria, typhoid, mumps, osteomyelitis and whooping-cough. The startling fact in these statistics is the high percentage of deaf-mutism which is caused by meningitis. It seems quite probable, moreover, that not a few cases of congenital deafness are cases where the loss of hearing has been due to meningitis acquired during the first year or two, that is, before the child has begun to speak.

Deaf-mutism results from total loss of hearing, but it may also occur in cases where "islands of hearing" are still preserved in the tone scale. When such islands lie between b^1 and g^2 they are of great value to the patient, since the fundamental tones for most of the consonants and vowels lie in this part of the scale. When even a slight hearing is preserved for the spoken voice, the patient can be taught to speak much more readily and satisfactorily than when no hearing at all exists.

Usually the functional examination of the labyrinth in cases of congenital deafness gives quite different results from those of the acquired. The reason is that in congenital deafness the developmental anomaly causing the defect in hearing is usually restricted to the cochlea and the saccule, while the utricle and semi-circular canals remain intact. In most cases of acquired deafness the destruction of hearing is dependent on a diffuse labyrinth suppuration, either from meningitis, panotitis of scarlet fever and measles or from suppurative otitis media. In these cases the function of the vestibule and semicircular canals is destroyed at the same time as the destruction of the cochlea. In most cases of congenital deafness, therefore, the functional tests disclose only a loss of hearing, whereas the semicircular canals give normal responses, and in acquired deafness the tests disclose a loss of hearing as well as a destruction of function of the semicircular canals. Bezold has found that only 20 per cent. of deaf mutes were totally deaf. It is possible to detect total deafness in a child as young as six months by standing behind the patient and watching for any reaction when loud sounds are made. Care must be taken that one is not being deceived by a response elicited by the jarring of the floor or a blast of air. To determine the status of partial loss of hearing cannot be done until the child is old enough to give intelligent responses.

Whether a deaf-mute is totally deaf or still possesses a remnant of hearing makes a vast difference. In the first place, cases of total deafness have the greatest difficulty in acquiring speech and the speech that is acquired in such cases is always extremely artificial and rasping, with relatively little that resembles human articulation. On the other hand, when a remnant of hearing exists, especially when this lies between b^1 and g^2, speech is much more readily acquired and the character of the voice is more nearly normal. A child that is totally deaf has a very noisy gait because he does not perceive the noise he is making. Moreover, where the total deafness is associated with a loss of function for the semicircular canals, as is the rule, the patient shows a characteristic slouchy, unsteady gait. Such cases can often be recognized as deaf-mutes by their manner of walking.

In the education of the deaf-mute it is of great importance to ascertain whether the patient is totally deaf or whether there is still preserved a remnant of hearing and especially whether this "island of hearing" lies between b^1 and g^2. It is always of great importance that the education of the deaf-mute should be undertaken at the earliest possible period so that the child may be taught to speak during the natural period for acquiring speech. The instruction must be largely individual, but the child will make greater progress, as a rule, if he is placed in an institution, where he receives the stimulation resulting from contact with other children undergoing the same training. In this country both state and private institutions exist for the education of these unfortunates.

CHAPTER CXC

OCULAR DISEASES OF INFANCY AND CHILDHOOD

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In this section there will be discussed at length only those anomalies and diseases of the infantile eye* that are of practical importance to the pediatrist and the general practitioner. The rarer eye disorders of childhood and a number of unusual congenital defects—although of interest to the ophthalmologist—really belong to ophthalmic monographic literature and these will only be listed or at most passed with brief mention. On the other hand, it is intended to dwell not only upon those conditions that are peculiar to children but upon those that while they also occur in adults are in early life so modified as to merit inclusion among essentially infantile affections.

ANATOMY AND PHYSIOLOGY OF THE INFANTILE EYE

The dictum of the older writers that the eye of childhood is a more delicate, more finely constructed organ than that of the adult is in some degree true. In a sense, the *ocular globe of the newborn* is small and undeveloped and, as a rule, does not grow to full size and assume normal conditions for several years. This fact explains, for example, the high degree of hypermetropia existing in many infants, because the short anteroposterior diameter of an eyeball is the usual cause of far sightedness in the adult; that is to say, it is found in eyes that do not develop or grow to normal measurements, thus entailing certain forms of eye-strain upon its possessor.

The *tissues of the infant's* eye partake, also, of the qualities discoverable in other infantile organs of mixed character, not to mention a peculiar structural delicacy that to a certain extent modifies pathological processes, produces symptoms and brings about alterations that, on occasions, widely differ from similar morbific conditions in the adult eye. The organic differences between the eyes of the infant and those of the adolescent will be considered briefly under the various subsidiary organs of the visual apparatus, as they are studied in this Chapter.

For convenience of reference and for the purpose of refreshing the memory of the student, several figures depicting the essential parts of the infantile ocular apparatus are given in the text.

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* For much of the text and many of the illustrations in this Chapter the writer is deeply indebted not only to the Cleveland Press but to the courtesy of his collaborators on the "American Encyclopedia of Ophthalmology."

The eyeball at birth is small and nearly round, although it varies considerably in size as well as in form. The average anteroposterior diameter is 17.3 mm. The period of most rapid growth, involving chiefly the anterior segment, is during the first years of life; this is followed by a period of slower growth, although the eyeball steadily increases in size up to the age of puberty. From the fourteenth to the twentieth year there is still another period of rapid growth, which involves the posterior segment. The cornea reaches its maximum measurement at the third year, although even during the first year of life the average diameter is not much less than that in the adult eye.

The *apparent size* of the eyeball depends more upon the width of the space between the lids than upon the length of its diameters. The prominence of the globe varies with the amount of orbital fat, but may be affected by disease.

Three coats, or tunics, are designated, *viz.:* An external, a middle, and an internal coat.

The *external tunic*, or tunica fibrosa, is composed mainly of dense, unyielding connective-tissue. It gives shape to the globe, protects the delicate inner structures, and resists intra-ocular pressure. About one-sixth of this coat is transparent, and is called the *cornea;* the remaining five-sixths, opaque and dull-white, are known as the *sclera*, or "white of the eye." With the exception of a round hole, the *foramen opticum scleræ*, near the posterior pole of the eyeball, incompletely closed by a sieve-like, perforated plate (the *lamina cribrosa*), this capsule is closed on all sides—disregarding, of course, the minute perforations for the transmission of vessels and nerves to the middle coat. Some authors, notably Thomson, of Oxford, refer to the cornea as an entirely separate structure imbedded in an anterior aperture of the sclera (*foramen scleræ anterius*).

The *middle coat* of the eyeball, or the *tunica vasculosa*, carries the vascular, nervous, and nutritive supply to the bulbar contents; it contains the muscle of accommodation, and is well furnished with pigment that lines the dark chamber of the globe and prevents reflections within it. In front, it forms a delicate curtain—the *iris*—pierced by an aperture—the *pupil;* posteriorly this membrane is known as the *choroid*. The tunica vasculosa, although lying close up against the sclera, is not actually connected with it, except at two places, *i.e.*, at the opening of the optic nerve (posterior insertion ring), and at the corneoscleral margin (anterior insertion ring). The capillary space extending between the two rings is called the perichoroidal space. A few blood-vessels and nerves cross it, and it is bridged by extremely delicate tissue lamellæ.

The *inner coat* is composed entirely of nerve tissue, and is called the retina.

The larger spaces, or chambers, within the eyeball are filled with fluid. That lying immediately behind the cornea is known as the *aqueous chamber*, and contains the aqueous humor. In fetal life a delicate membrane covers the pupil, completely subdividing the aque-

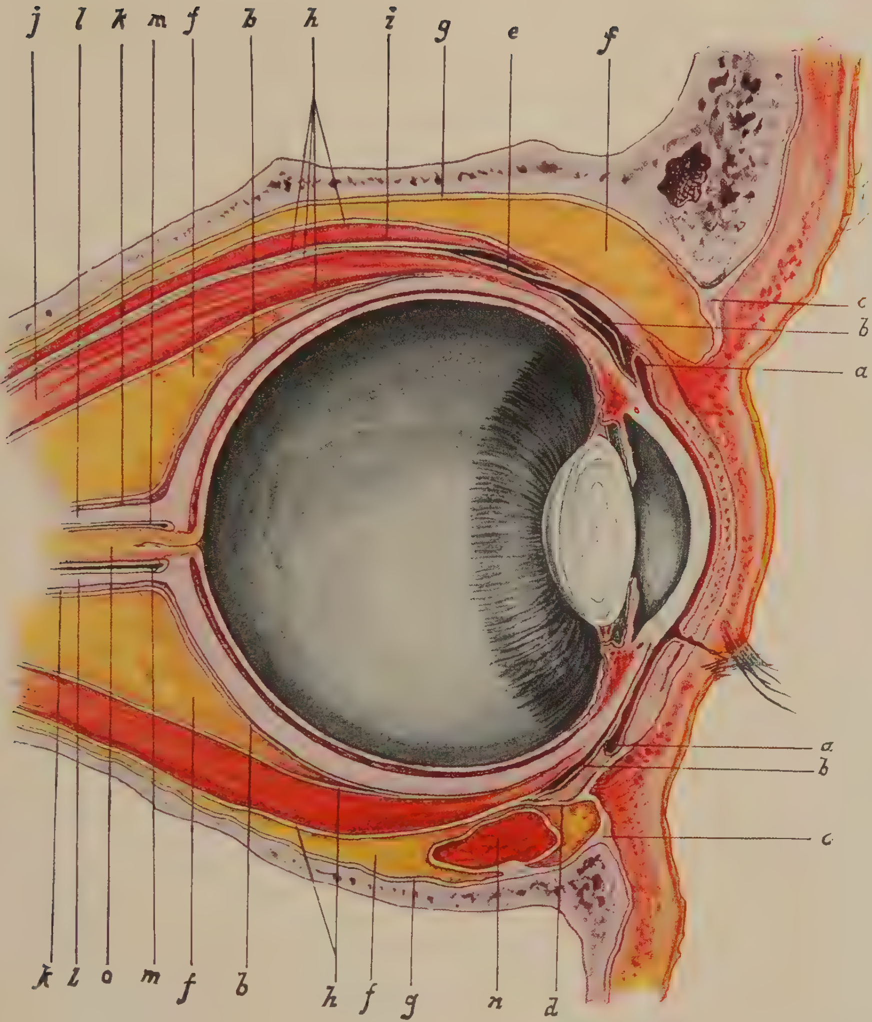

FIG. 95.—Vertical section of the eye in the orbit: *a*, Conjunctival fornix; *b*, capsule of Tenon; *c*, orbital septum or orbitotarsal ligament; *d*, check ligament of inferior rectus; *e*, connection between superior rectus muscle and levator palpebræ superioris muscle; *f*, fat; *g*, periosteum of orbit; *h*, orbital fascia; *i*, levator palpebræ superioris muscle; *j*, superior rectus muscle; *k*, supravaginal lymph space; *l*, fibrous sheath of optic nerve; *m*, intervaginal lymph space; *n*, inferior oblique muscle; *o*, optic nerve. (American Encyclopedia of Ophthalmology, Vol. I.)

ous space into an anterior and posterior chamber; after birth the pupillary membrane disappears, and the two spaces communicate through the pupil. The large space back of the lens is filled with a gelatinous fluid called the *vitreous humor.*

EXAMINATION OF THE EYES OF CHILDREN

The ocular apparatus (Figs. 94, 95) of infancy differs little from the adult eye except, of course, in the greater delicacy and immaturity of the component tissues. In that respect, therefore, the procedure in a physical examination is practically the same. On the other hand, that the practitioner may gain as much information as possible from an injury into the state of a child's eyes it is well to remember that he must carry out his observations with due regard to the fact that reliance must be placed on *objective methods* alone. Suggestions leading to

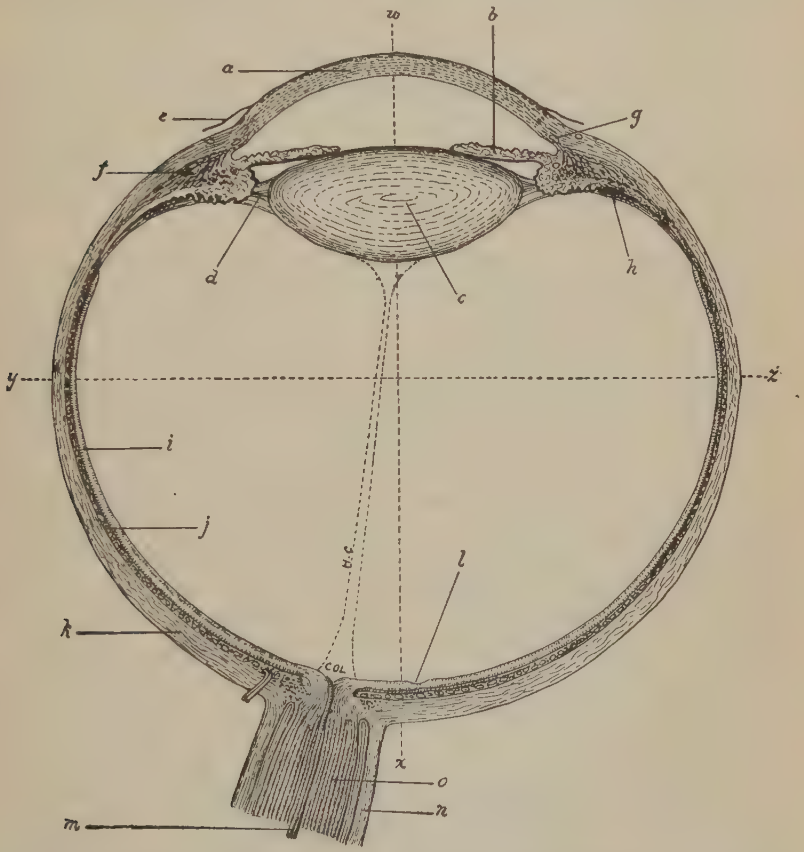

FIG. 94.—Section of the eyeball. *a*, Cornea; *b*, iris; *c*, lens; *d*, zonula of Zinn; *f*, ciliary body; *g*, canal of Schlemm; *h*, retina; *j*, choroid; *k*, sclera; *H. C.*, hyaloid canal; *l*, macula; *o*, optic nerve; *w*, anterior capsule. (After Quain.)

a diagnosis may be had from parents or nurses but not much value can be placed upon them. While young children differ greatly in the degree of assistance they give the examiner yet in most instances the successful pediatrist relies, even when his patient has reached the age of seven or eight, on his own powers of observation; and these usually take the form of *simple inspection* supplemented by the aid of *instruments,* in an orderly examination of the eyes of juveniles.

First of all, then, the examiner should ask himself, what is to be seen by *general inspection of the ocular region?*

The first and most important thing to be considered in the objective examination is *the illumination of the patient.* The ordinary examination of the eye for the purose of making a diagnosis is best accomplished by the use of good, clear daylight from a window, facing which sits the patient. The surgeon stands in front of the patient, so adjusting his person that no shadow is thrown on the subject, but in such a position that he can examine the part thoroughly.

The chair in which the patient sits should be of the proper height, so that the surgeon may comfortably see directly into the examined eyes.

Eruptions on the skin should always be observed and are of great significance. Eczema, pityriasis, herpes zoster and other skin diseases may affect the lids as well as other parts of the body. Syphilitic eruptions, if observed at the same time we diagnose a case of iritis, satisfies us immediately that the disease is a specific one. The hue of the skin may give important hints as to the condition of the blood.

The directions given by Rochester* for a *systematic objective examination of the eye* itself may well be abstracted here. He suggests that the observer begin by *observing both eyes simultaneously and comparing one with the other.* The size of the palpebral openings is noted and any inequality is quickly discerned. If an orbital or brain tumor be present causing exophthalmus or lateral displacement of the globe, these conditions are much more easily detected by a comparative examination of *both* eyes. Such marked difference as the absence of one eye; a turning of the globe; the presence of an inflammatory swelling, or the existence of a tumor or ulcer, will immediately be noticed.

Next centering attention on *one eye* the surgeon first observes the condition of *the eyelashes;* whether they are present in normal number and evenly distributed along the margin of the lid. Notice should be taken of the direction of the cilia; if they turn toward the globe, and are improperly directed (*trichiasis*) or if they are present in two or more rows (*distichiasis*).

Search should be made for small, white, downy hairs, which may grow from any part of the lid margin, and are often found at the inner canthus, where they rub the globe or caruncle at every winking act. "Wild hairs" which are short, thick and black, often cause much irritation. Parasites (*phthiriasis oculorum*), may be found at times about the roots of the cilia. If the lashes are found matted together with a moist substance, it at once suggests the presence of some form of conjunctivitis.

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* "American encyclopedia of ophthalmology," vi.

After the eyelashes the next step is to examine *the lids.* They should be carefully observed as to color, mobility and thickness. The mouths of the Meibomian glands, at the edge of the lids as well as of the tarsal cartilages, are carefully examined. A localized inflammatory swelling of the lid will suggest trauma, hordeolum, erysipelas, erythema, sarcoma, an inflamed chalazion, or acute circumscribed edema. A local, non-inflammatory swelling may be due to a dislocated lachrymal gland or a chalazion. If it be the latter a hard, round body, like a shot, will be felt. A local, non-inflammatory swelling may also be due to nephritis. A general inflammatory swelling of the lids is met with in trauma, gonorrheal conjunctivitis and erysipelas. A general non-inflammatory swelling may be caused by emphysema, in which case palpitation will elicit the characteristic crepitation; or it may come from the accidental discharge of a solution which has been thrown into the cellular tissue while injecting the naso-lachrymal duct.

The puncta should be examined for permeability, pressure at the same time being made over the lachrymal sac in order to express from it, through the puncta, any contained fluid.

The contour of the lid may be changed by scars from wounds, ulcerations, or burns. The finger should be passed over the lower part of the anterior surface of the upper, and corresponding portion of the lower lid, to feel for thickened areas. If present, they suggest tarsitis or occlusion of the Meibomian ducts.

Having completed this general survey of those external parts of the lids which are easily seen, the examiner next proceeds to the *inspection of the conjunctiva lining the inner surface of the lids.* To do this he must evert both lids so as to bring these parts into view. This is very easy of accomplishment so far as the lower lid is concerned. The patient is told to look up and while he is doing so the examiner pulls down the skin of the lid with the tip of one finger in such a manner as to cause the palpebral conjunctiva and the conjunctiva of the lower fornix to roll out into plain view.

Very often on *examining the eyes of infants,* in whom the lids have become edematous and swollen from crying or other causes, simple separation with thumb and finger will cause the lids to evert themselves and completely expose the inner surfaces.

Eversion of the lids—especially of the upper lid—of small children had, however, better be postponed *until the end of the seance,* as after it has been thoroughly and properly accomplished the patient is generally so excited (though wholly uninjured) that further examination of the eyes by inspection is often difficult or impossible. However the method most successfully employed is the following and it is strongly recommended as a humane, painless and effective means of *inspecting the external eye, eyeball and conjunctival sac,* and is far preferable to the vain attempts sometimes made to gain information by examination in the upright position, employed for adults. It consumes but little time and is available for most infants and children under six years of age.

The surgeon sits facing the nurse, who holds the child firmly in her lap by grasping its hands and legs. The child's body is in a horizontal position, the head being toward the examiner and resting between his knees. By pressing the knees tightly against the patient's ears he holds the head securely, allowing both his hands to be free for manipulating the lids. Children are often terrified and may struggle, so it is well to be very careful to avoid pressure on the globe. Often by simply waiting until the child becomes tired, one is able easily to examine its eyes. However, in some cases with an affection of the conjunctiva or cornea, producing photophobia, or if there is great swelling of the lids, it may be necessary to use the ordinary lid elevators. Usually one instrument is sufficient, being introduced under the upper lid, while the thumb of the surgeon pulls down the

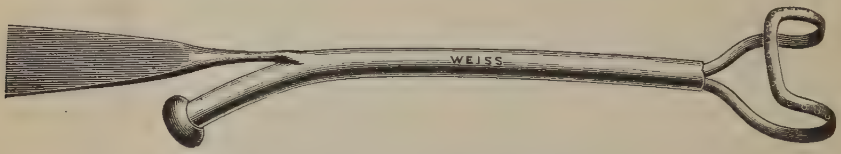

FIG. 96.—Edgar Brown's eyelid retractor and douche combined.

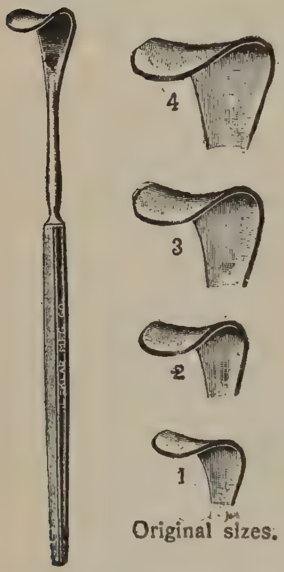

FIG. 97.—Desmarres' lid retractor (four sizes).

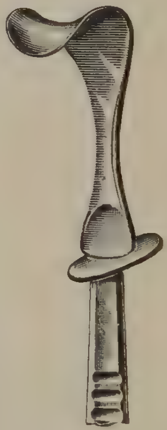

FIG. 98.—Lid elevator of Kramer.

FIGS. 96–98.—Various forms of lid retractors with and without combined douche.

lower lid. Great care should be exercised in placing the lid hook in position, for, if the cornea be ulcerated and undue pressure be excited, it may be ruptured and the lens evacuated.

The so-called *secondary eversion of the upper lid* is a manipulation which is often omitted, but is of great value in some cases.

It exposes the retrotarsal fold, but requires some skill to accomplish without instrumentation. The edge of the everted upper lid is pressed firmly against the supraorbital margin with the thumb of the left hand; then push the lower lid upward over the cornea with the right index finger, at the same time exerting gentle backward pressure upon the eye-ball.

The best instrument for accomplishing this is the Noyes retractor. After turning the upper lid in the ordinary manner the retractor is passed beneath the everted lid so that the lip of the instrument passes into the upper fornix. We now have exposed a region which is a favorite seat of trachoma and a nidus for foreign bodies. Papillary tumors of the conjuctiva occasionally grow from this part, owing to the irritation caused by the lodgment of a foreign body

After observing thoroughly the condition of the conjunctival surfaces of the lids, looking carefully for any change in smoothness, thickness, or secretion of this membrane we proceed to the *ocular conjunctiva.* One first notes if any undue redness is present, and, if present, whether it is greatest posteriorly, in the region of the fornices, or anteriorly, around the corneoscleral junction.

For *thorough cleansing of the conjunctival sac and the proper application of remedies* it is absolutely requisite to expose the parts. For this reason the above mentioned method is generally employed in young children, and particularly in such instances as ophthalmia neonatorum or ulcer of the cornea. When topical remedies are exhibited the greatest gentleness and dexterity of manipulation are required.

In such cases smooth, rounded lid retractors are the only ones permitted.

The condition of the *lachrymal apparatus* should next be observed by the examiner. The puncta should be carefully examined as to the presence or absence of a foreign body, such as stray eyelash. Notice whether the puncta are directed properly, so as to take up the flow of tears. In the normal position, it is not possible to see a punctum except on lifting the lid away from the eyeball.

Palpation reveals the condition of the tear-sac. If on pressure we cause a discharge of pus or mucus into the conjunctival sac above or, less frequently, into the nose below, we may feel assured that the sac is diseased. If there is doubt as to the patency of the drainage apparatus, a small amount of warm boric acid solution may be injected into the lower canaliculus from a hypodermic syringe armed with a blunt needle. If the fluid runs freely into the nose we may assume that the drainage system is clear. But if the fluid returns into the conjunctival sac by way of the upper canaliculus there is either an obstruction or stricture.

Another method of testing the condition of the lachrymal passages is to place several drops of a 2 per cent. fluorescein solution on the conjunctiva and then after waiting several minutes have the patient blow his nose into a clean handkerchief. The solution will, if the passages are clear, have passed into the nose and will be found as stains on the handkerchief.

The accessory lachrymal gland may be seen by drawing the upper lid well away from the globe and at the same time having the patient look downward. Under normal conditions the gland proper cannot be seen or felt.

Having now completed our examination of those structures immediately surrounding the eyeball itself, we begin *observations of the globe* by turning our attention first to its position in the orbit. A marked protrusion of the globe, or *exophthalmus*, is easily noticed, but a slight one is not readily distinguished, particularly if it involves both eyes. In cases of slight protrusion where it is a question whether a pathological condition is present, accurate measurements should be taken with an exophthalmometer. These can be repeated from time to time and by comparison of the findings valuable deductions made.

Hertel has devised an *exophthalmometer* which measures the position of the eye-ball accurately and rapidly. The instrument is fitted with two movable mirrors and scale carriers with sleeves by which they may be slid along a guide bar and accurately set to the outer margins of the orbital cavities of the patient's eyes. The distance between these margins is shown by the scale on the guide bar. Every time a fresh measurement is taken the instrument may be quickly set by the scale. The operator looks with both eyes into the left or right pair of crossed mirrors. The lower mirror shows the lower half of the vertical profile of the cornea turned round into a plane at right angles to the observer's line of sight, whilst the upper mirror forms an image of the scale for measuring the protrusion of the cornea in approximately the same plane in which the profile of the cornea is seen; the two images are accordingly seen without any appreciable amount of stereoscopic parallax. In the event of the corneal apex being situated exactly 20 mm. nearer to the meridional plane than the points where the instrument rests on the orbital margins the plane of the scale image and that of the corneal profite are strictly coincident. The reading gives the distance in millimeters from a frontal plane passing through the points of application on the orbital margins.

It is often advisable to examine the *sensibility of the cornea.* This procedure is best accomplished by gently touching the surface of the membrane with a wisp of cotton twisted to a fine point. If sensation be normal, the touch should be instantly followed by the reflex act of winking (palpebral reflex), although even when the cornea is insensitive, closure of the lid may occur if the test-object comes in the field of the pupil. This is not due to contact, but represents the *retinal* lid-closure reflex.

Minute abrasions and ulcers of the cornea, if suspected and yet not determined, may be found by dropping on the eye a concentrated alkaline solution of fluorescein (fluorescein, 2 per cent.; carbonate of soda, 3.5 per cent.), allowing it to be absorbed for several minutes and then thoroughly irrigating the cornea with a boric acid solution. If any portion of the cornea is deprived of its epithelium, or any part of the corneal epithelium is diseased, it will be found to have retained a yellowish-greenish stain, while the healthy epithelium remains unaffected. However, there is one exception, in that the epithelium in the immediate neighborhood of a corneal ulcer, which, although apparently not involved in the process, will also take the stain to some extent.

The most useful of all examinations of the cornea is that carried on under *oblique illumination*. By it we are able not only to ascertain to a certainty the condition of the surface, but by focusing our point of light lower and lower we expose layer by layer all parts of the cornea as well as the anterior chamber, iris and lens. This procedure should be carried on preferably in a darkened room with a very clear, bright, artificial point of illumination. The room should have dead black walls and should receive no illumination except that cast by the light the surgeon uses. The light which is now most popular is the electric lamp with a frosted globe; although the Argand gas burner was generally used a few years ago.

By means of a strong convex lens of 2 or 3 in. focus light is concentrated on the eye in such a manner that the apex of the cone of light corresponds to the part to be examined. *The source of illumination should be about* 18 *in. to the side of the patient*, several inches in advance, and on a level with the eye. The lens is held by its margin between the thumb and index finger, so that its surfaces are at right angles to the direction from which the light proceeds, and steadied by means of the little finger placed against the side of the patient's face.

The *anterior chamber* should be examined under the oblique illumination as to its depth, the clearness of its contents, and the possible presence of a foreign body or an exudation. The depth is observed by noting the relationship of the iris to the posterior surface of the cornea. If the chamber be shallow and the iris is bulging forward, this fact is often best established by looking at the eye-ball from the side. Normally, the anterior chamber is shallower in infants and in the aged than in middle life.

In a healthy state the aqueous humor is absolutely transparent and therefore not seen at all. In disease, however, it may be mixed with pus, blood or lymph, when it becomes opaque. Fluids in the anterior chamber gravitate according to the position of the patient.

After completing a thorough inspection of the cornea and anterior chamber, the surgeon should begin his *examination of the iris*. The color of irides is found to vary greatly. Blue and gray are the predominating hues in northern countries; brown is found next in frequency; while the various mixtures produce yellow and green shades. Absolutely black irides are never encountered; but dark irides, taking into account the whole population of the world, are of the most frequent occurrence. The color of the iris of all newborn children is a light grayish-blue (de Schweinitz). It is only as the pigment later becomes formed and deposited, that the iris assumes its permanent color. The location and amount of pigment decides the shade of the iris. If the pigment is deposited more freely in the posterior layer than in the stroma, the blue iris is evident. If, however, the stroma receives the major amount of pigment the iris is brown or dark-brown. Piebald irides are often seen and are due to an irregular deposit of pigment, sometimes appearing as one triangular patch or several irregular spots of dark color. This condition is sometimes temporary. Some of the very small, dark segments in piebald irides much resemble foreign bodies and have even been diagnosed as such by competent surgeons.

Discoloration is an important indication in disease of the iris and should always be carefully looked for. If one iris presents a more greenish hue than its fellow, it may be taken as a sign of beginning iritis or cyclitis. It is to be remembered, however, that in health we occasionally find two irides in the same individual, of an entirely different color (heterochromia). If tremulousness of the iris can be elicited by having the patient move the eye rapidly about, it indicates a lack of support and is found when the zonula is relaxed or the lens absent, dislocated or shrunken.

The pupil next commands attention and the examination is most important. The size is first noted and this varies greatly even in health. Exposure to light or darkness causes variations in its size as well as the performance of the acts of accommodation and convergence. Also its width depends on the quantity of blood in the vessels of the iris, the elasticity of the iris-tissue, and certain mechanical conditions. According to Schwarz, the normal pupil may undergo fluctuations in diameter amounting to 0.3 mm., even when the chief factors are practically constant. In general, the pupil is smaller in eyes with a hyperopic refraction, in old age and in the newborn; while in myopic eyes and in the eyes of youth they are found larger. Men usually have narrower pupils than women. In absolutely normal eyes, with the accommodation at rest, the pupil varies in daylight from 2.44 to 5.82 mm., the average diameter being 4.14 mm. (Woinow). The position of the pupil is a little to the nasal side of the center of the cornea.

The pupils of both eyes in health should be the same size when exposed to the same degree of illumination. In very rare instances this is not true, for slight inequality has been seen in healthy persons, and may be a congenital condition.

Many instruments known as *pupilometers* have been invented for accurate measurement of the pupil's size. The simplest design is made of a small, round sheet of black metal, with holes of different sizes punched in it. The instrument is held close to the eye and rotated until the hole is found which matches the pupil in size. Priestley Smith's keratometer may be also used for this purpose. Haab has constructed a practical pupilometer, which consists of a number of black discs, varying from 1.5 to 8mm. in diameter, arranged in a perpendicular row, with which the pupil is compared.

With a little patience and if they are applied early in the examination many of the *pupillary reflexes* can be elicited even in quite young children. The methods of eliciting these does not differ from those applicable to adults.

The pupillary area, which is next examined, should be first scrutinized by oblique illumination. Search is made for posterior synechia or any evidences on the anterior capsule of that condition having previously existed. The latter would be shown by pigment-spots or points of exudation on the capsule.

Proceeding deeper, the surgeon examines *the lens substance* itself by *oblique illumination*. In order to do this satisfactorily it is necessary to have the pupil well dilated. One or two drops of a 4 per cent. solution of cocain instilled into the eye, is a very satisfactory mydriatic for this purpose, as its action lasts only for a short time. Opacities or foreign bodies are looked for. Opacities when seen by oblique illumination appear grayish on a black background. When later we observe them with the ophthalmoscope they take on a much different appearance, being black on the red fundus reflex. Foreign bodies are easily seen, but usually they soon set up a rapid swelling of lens substance which obscures them. Occasionally, however, a small body may lodge in the lens substance and remain there for years without giving rise to any trouble.

The examination of the lens is also made by the surgeon with the aid of the ophthalmoscope.

If the lens is quite clear, the anterior part of the vitreous may be seen by the oblique method but the most practical and valuable observations of the vitreous body must be carried out by the ophthalmoscope.

The intraocular tension is of importance and should be determined in every eye examined. As a rule it is increased in glaucoma, intraocular tumors and sometimes in iritis. It is decreased as a rule, in detachment of the retina, perforation of the globe, liquefaction of the vitreous humor, and in pseudo-neuro-epithelioma.

When observing the tension of an eye the usual method, and the only one applicable to children, is that simple procedure of palpating with the index fingers, much in the same manner as one detects fluctuation in any other part of the body. This method is quite satisfactory in most cases, and the trained observer, after long experience, is able to detect the slightest alteration from normal; whether it is an increased or decreased tension. The tips of both index fingers are placed on the upper eyelid and the middle and ring fingers are allowed to rest lightly on the brow; now by alternately directing pressure downward onto the eye-ball by first one finger and then the other, the exact condition is determined. It should always be remembered to exert the pressure downward and not backward, for a backward pressure would to some extent only press the globe into the orbit and the results arrived at would be misleading.

The condition found in one eye should always be compared with that of its fellow, and if there be any doubt the results should be contrasted with those obtained by examining the normal eye of an individual of the same age

The findings by the palpating method, just described, are expressed very simply. T*n*. indicates normal tension, and departures from normal are expressed by the symbols +1, +2, +3 and −1, −2, −3; the plus sign showing increased tension (hypertony). Roughly translated, +1 means tension noticeably increased, +2 greatly increased and + 3 hard as rubber. The minus terms indicate diminished tension (hypotony); −1 meaning a noticeable decrease, −2 great decrease and −3 an eyeball that is distinctly soft.

The *determination of the amount of vision* (*visual acuity*) is often of great importance. This really subjective test should be applied before the objective examinations are made.

By *visual acuity* we mean the ability of the eye to distinguish size and shape. The *refraction of the eye* and visual acuteness are frequently confounded. They are two entirely different things, however, and should be clearly distinguished from each other, although in practice we are accustomed to determine them together. The refraction is simply a state of the dioptric apparatus; while the visual acuity is largely a condition of the nervous apparatus of the eye.

The results of numerous experiments have shown that the two points of a retinal image, in order to be clearly distinguished from each other, must be separated by a distance of 0.00436 mm. Such a retinal image corresponds in the normal emmetropic eye to a visual angle of 1. Therefore, it is a measurement of the visual angle for objects (generally letters) that establish visual acuity.

The *test most used for illiterate children* is that of figures resembling the Snellen "E." These figures are turned in different directions (much as the Landolt rings) so that the openings point either up, down, left, or right.

An object test card, or kindergarten card for visual tests has been devised by Reber* using objects likely to be recognized by young children, and conforming as nearly as practicable to the test letters used at six meters.

Apart from its scientific interest, it is often of great practical importance to be able *to estimate approximately a young child's visual acuity*. Worth accomplishes this by means of five ivory balls varying in size from ½ to 1½ in. in diameter. The child is first allowed to handle the balls with both eyes open. Then one eye is covered by a pad, or, if he wears glasses, by a piece of cotton wool stuffed behind the lens.

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*Jour. Am. Med. Ass'n (Dec. 16, 1911), p. 1993.

He is then asked to go and pick up the balls as they are thrown on the floor to a distance of 6 or 7 yd. one by one, beginning with the largest. By spinning the ball in the fingers as it is thrown, it may be made to "break" on touching the floor, so that it does not go quite in the direction in which it appeared to have been thrown. It is easy to tell, by the way in which the child runs for the ball, whether he really sees it before he starts or is only going to look for it.

In connection especially with suspected *squint* or *paresis of the eye muscles* three conditions are to be investigated when examining *the motility of the eyes.*

First (when the eyes are at rest), we note the relation of the optic axes to each other. Second, we examine the ability of the eyes to preserve the proper relationship of the optic axes so that binocular single vision may be realized. This is the "fusion power." Third, we ascertain the voluntary power of the eyes to rotate in various directions.

There are (as in determining the ocular tension) numerous instruments for registering the occurrence and degree of defective ocular excursions, but none of these are of much value in the oculo-muscular anomalies of young children. For them the following simple methods are preferable.

The cover test or screen test is applied by having the patient look at some small object held about 15 in. from the eyes. A card is placed alternately over one eye and then over the other, while the surgeon observes the position and movement of the eye at the instant of uncovering. A movement inward indicates that the eye has deviated outward (*exophoria*). A movement downward means *hyperphoria.*

In *the fixation test* the patient is told to observe the surgeon's finger, which is slowly advanced to within 3 in. of the patient's nose. If one eye turns out, there is exophoria. This test is a rough one, and its chief value is in determining which of the interni is the weaker.

The *refraction of children's eyes* is closely related to the ocular hygiene of early life.

The normal child is born hypermetropic but without much astigmatism. The myopic child is either defective from birth or (much more frequently) has acquired myopia from the stress of eyestrain, generally through the "turnstile of astigmatism." Astigmatism (abnormal curvature of cornea or lens or of both) may be congenital, but is sometimes acquired in the normal child during the early years of life by excessive strain on the muscles of accommodation.

Kindergarten and primary work should be arranged so as to avoid strain on the muscles of accommodation of the eye, in the plastic years of childhood. Hence, early school work and all other wearying exercises should be limited in amount, if not absolutely eliminated.

Systematic study should be begun only when the delicate and soft tissues of the child's eyes have sufficiently developed to resist distortion on moderate use of the accommodation. This means that prolonged close work should not be allowed until the age of 10 or over. A child beginning systematic study at that age will, with suitable care, be able at 16 or 18 to acquire all the knowledge possible to its more precocious companions, and will have the inestimable advantages of normal eyes and healthy physique. No young child should be encouraged to compete with its companions for prizes. Mental and ocular overstrain are the inevitable results of such educational monstrosities. In the primary schools especially there should be no grading of the children.

A child incapable of prolonged use of the eyes at the proper age should not be classed as "lazy" or "stupid." In the majority of such cases there will be found uncorrected refractive errors.

Inability to concentrate and deficient powers of observation are often caused by poor visual memory the result of eye-strain.

The symptoms and physical signs of *eye-strain* in children can be easily recognized, and there is no more brilliant success in medicine than that which follows the correction in children of refractive over-strain.

For the *measurement of the total* amount of refractive error—*ametropia*—in infants and children, by far the most valuable means is that of *skiascopy*—the so-called "shadow test." By this method exact information is obtained as to the static refraction, the *kind of glasses to be ordered* to improve vision or to relieve eye-strain, etc. in even the youngest subject, but as it is a procedure requiring special knowledge and much practice—and consequently belongs to the domain of the trained ophthalmologist—no attempt will be made to describe its *modus operandi* in these pages. Indeed the whole question of the prescription of glasses in early childhold is so important that it should be decided only by a specialist in ophthalmology, particularly as it is now well recognized that *no child is too young to wear glasses if he needs them.*

The *state of the interior of the eye*, especially the condition of the choroid, retina and optic nerve is determined by means of the *ophthalmoscope.* For restless children the so-called *indirect method* is the most satisfactory, although both it and the "close-up" or *direct* method should be employed.

In the opinion of the writer every pediatrist should have a working knowledge of the valuable aid to diagnosis and treatment furnished by ophthalmoscopy, and he should not abandon its employment entirely to the ophthalmologist. For this reason a few paragraphs will be devoted to the subject.

Examination of the eye by aid of the ophthalmoscope may be divided into four divisions. (1) Ophthalmoscopic examination for determining the refraction of the eye. (2) Ophthalmoscopic examination with the instrument at a distance for exploring the media of the eye-ball. (3) Indirect ophthalmoscopy, for a general examination of the fundus with low power magnification. (4) Direct ophthalmoscopy, for examining minutely the fundus with a greater magnification.

Methods of Using the Modern Ophthalmoscope.—As the chief purpose of an ophthalmoscopic examination is to see as much as possible of the interior of the eye under observation it is desirable to dilate the pupil; this is accomplished by instilling into the eye atropin, homatropin, euphthalmin or some other mydriatic.

Before the invention of the self-luminous or electric ophthalmoscope the source or illumination of the ocular interior was a gas jet or electric bulb—preferably an argand lamp—stationed in a darkened room, and placed on a level with the eye to the side of the head.

In examinations of the human eye the observer sits opposite the individual whose ocular interior is to be explored, and placing the mirror close to his own eye and about 40 or 50 cm. from the eye to be examined reflects the light upon the latter, while he looks at it through the small opening in the ophthalmoscopic mirror. In very short-sighted and very long-sighted eyes, but not in normal ones, the vessels of the retina, the entrance of the optic nerve, etc., can be more or less distinctly seen.

The details of the retina, choroid, etc., can be seen in two different ways. By the *indirect method* the observer holds a strong convex lens about 10 cm. from the eye under examination, and between it and his own, when a clear, real image of part of the fundus, inverted and magnified about four diameters, appears in the red light of the pupil.

In the *direct method* the observing eye must be placed as close to the observed as the intervention of the mirror will allow, when a virtual image of a still smaller part of the fundus is seen, but erect and magnified about 14 diameters.

By means of the electric self-illuminating ophthalmoscope one is enabled not only to dispense with the cumbersome side light but to make satisfactory examinations of the fundus oculi in only partially-darkened surroundings—serious considerations in doing house and hospital-ward work.

The fact that a considerable portion of the light thrown into the interior of the eye through the pupil is reflected by the structures of the background into the eye of the observer is the principle of the ophthalmoscope. Moreover, this reflection, or rather refraction, of the incident rays, modified by the character of the media through which they pass furnish the wonderfully varied and colored pictures observed in the ocular background.

Perimetry in Childhood.—In some cases of older, intelligent and docile children the limits of the visual field may be *roughly* mapped out. Instrumentation is of little value, if for no other reason than that the employment of the perimeter is fatiguing, requires considerable time and patience and is generally unsatisfactory. A simple and often sufficient procedure is the following: Place the patient with his back to the source of light, and have him fix with the eye under examination (the other being covered) the center of the eye of the observer, which is directly opposite his own, at a distance of two feet. Then let the surgeon move his fingers in various directions midway between himself and the patient, on a plane with his own face, until the limits of indirect vision are determined, controlling, at the same time, the extent and direction of the movements by his own field of vision.

This method suffices to discover any considerable limitation, and, in the event of such discovery, should (when possible) be supplemented by a more exact procedure.

THE OCULAR COMPLICATIONS OF THE PRINCIPAL DISEASES OF INFANCY AND CHILDHOOD

Of these, the commoner *acute exanthemata* are the most important. For the purposes of this section they may be listed as measles, scarlatina, chicken-pox, vaccinia, small-pox, cerebrospinal meningitis, typhoid, and diphtheria.

The *serious ocular diseases of infancy and childhood, i.e.*, those that produce blindness, are given in the tables of Magnus, whose first group covered the period from birth to the age of 15, and the figures give the percentage of lost vision in each disease:

Glioma retinæ	1.52
Measles	2.66
Scarlet fever	2.66
Small-pox	4.18
Typhoid fever	2.28
Other acute exanthemata	1.90
Atrophy of the optic nerve	15.58
Detachment of the retina	2.28
Various other retinal diseases	2.66
Diseases of the uveal tract	7.22
Diseases of the cornea	8.36
Sympathetic ophthalmia	6.08
Traumas	1.52
Conjunctivitis diphtheritica	0.38
Trachoma	0.76
Blennorrhea neonatorum	38.78

A *complete list* of the eye diseases peculiar to infancy and childhood include the foregoing diseases as well as congenital anomalies and the transient and less serious affections of the infantile visual apparatus, many of them the sequelæ of diseases mostly encountered in early life.*

The *pathology, prognosis, and treatment* of many of these diseases are but a part of (underlying) conditions extensively and fully treated in other chapters of this work. Consequently they will, to avoid needless repetition, be passed over with a reference to the parent section.

Dutoit† finds that in the *chronic infectious diseases of children*, due to syphilis, tuberculosis and influenza, this is well worked out, while the eye complications of acute infectious diseases are rarely mentioned in literature. He attributes this to the fact that acute infectious diseases, especially of children, are mostly treated at home and therefore are not systematically examined with the ophthalmoscope. A certain number of such cases escape observation, as they frequently occur in children who generally do not complain of defect of function. Also, infectious optic neuritis occasionally affects only one eye, so that the impairment of vision may not be noticed. Finally, the favorable course of exanthemata contributes to its apparent latency.

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* The writer is largely indebted, in the following pages, to excerpts and illustrations from the "American encyclopedia of ophthalmology," edited by himself.

† Archiv f. Augenheilk., lxxi, p. 1.

Uhthoff believes that in cases of *optic neuritis after measles, scarlet fever and typhoid,* meningitic complications through increased intracranial pressure may cause choked disc, which arouses the erroneous impression of a specific optic neuritis. Dutoit says that this can be easily decided by lumbar puncture, and other diagnostic methods of internal medicine and by certain peculiarities of meningitic choked disc (e.g., involvement of the intermediate zone) in comparison with papillitis from infectious or toxic causes. The analysis of the urine is very important in deciding the etiology of some forms of toxic papillitis, and even more in optic neuritis with such endogenous infections as albuminuria, diabetes mellitus, etc. Rise of temperature is also a determining factor in separating infectious optic neuritis from toxic neuritis.

As a proof of his views, the writer reports the clinical histories of two cases of *optic neuritis after measles*, one after *scarlet fever*, and one after *typhoid*. The optic neuritis occurred late, from 15 to 20 days after the onset of the general disease, and thus had the character of a paraspecific affection. The diagnosis of paraspecific optic neuritis and its discrimination from meningitic papillitis rest on the negative result of lumbar puncture, the clinical observation in general, and on the, although not quite conclusive, ophthalmoscopic examination. Meningitic papillitis and choked disc are characterized by more or less prominence and considerable enlargement of the optic disc in all diameters, due, according to Schieck and Kuhnt, to a swelling of the intermediate tissue, which under normal conditions is invisible. The pathogenesis of paraspecific optic neuritis has nothing to do with increased cerebral pressure and is not brought about in a mechanical way, so that there is no constriction-choking of the disc nor imbibition of the intermediate tissue.

The predisposition to paraspecific optic neuritis in these cases is due to diminished power of resistance in consequence of the retarded reconvalescence. The remarkably favorable course of all cases under treatment with emulsion of cod-liver oil was, according to Dutoit, encouraging, and Dutoit recommends it for further trials.

In two cases of *influenza* the optic neuritis set in with fever and symptoms of a more or less manifest cerebral irritation. Lumbar puncture was negative.

The writer considers optic neuritis as a coördinate manifestation or localization of influenza. The affection of the optic nerve leads, according to its intensity, to some general phenomena which are partly signs of a hematogenous infection, partly of cerebral irritation.

From the favorable course of his cases the writer believes that in the papillitic form of infectious optic neuritis the prognosis is good.

Eye Affections in Measles.—Like all infective general diseases, measles may cause complications which are often benign, but occasionally assume a grave character. When the eyelids are involved, the same characteristic splotches are present as occur in other parts of the skin. A mild conjunctivitis, in the scant secretion from which the staphylococcus and the streptococcus are sometimes found, occurs in almost every case of measles, usually just preceding the rash. The lowered power of resistance of the system permits the invasion of other parts by these microorganisms, and various infective processes may develop (see, also, "*Gangrene of the lids,*" in this Chapter).

In 1901 Trantas (Constantinople) published his observations upon the *condition of the cornea in cases of measles.* He found superficial punctate keratitis to be a very frequent symptom of the disease; it was present in 76 per cent. Morax, in 1903, stated that he had carefully examined 27 cases of the diseases in Paris, and in these he had found no sign of such corneal disturbance. On the contrary, he constantly found "a hypersecretion of the glands of the ciliary margin" which produced small gray masses; these were deposited upon the corneal epithelium, and suggested the lesions described by Trantas.

A rare case of acute *diffuse choroiditis* following measles is reported by Mikami. The fundus showed diffuse depigmentation and haziness, and small white spots at the periphery. He attributes the condition to bacterio-toxic influences.

Among the more serious ocular complications of measles, manifestations in the central or peripheral nervous system are important. *Optic neuritis* is the most frequent as well as the most serious of these. Von Graefe first reported a case of optic neuritis after measles in 1866. Griscom* has been able to find reports of only 23 cases of *blindness due to optic nerve lesions following measles.* The cases may be divided into three classes; first, those showing evidences of primary cerebral involvement with secondary optic nerve change; second, those showing meningitis as the most prominent symptom, with consequent optic neuritis; and third, those showing optic neuritis without any other local or general symptoms. In these cases there may be a circumscribed meningitis in the region of the optic nerve or the neuritis may be due to the selective action of the toxins of measles.

In a case of his own, that of a girl of 11 years, the right eye became blind a week after a light attack of measles, and in a few days the left eye was likewise involved. After persistent treatment vision began to improve and in eight months reached 20/20 in each eye with full visual fields. The edematous swelling he attributes to the irritating toxins circulating in the blood, and not to a true inflammatory condition.

Santos Fernandes† reports the case of a girl of seven years who lost her vision after the disappearance of the eruption of measles. The pupil was fairly well dilated, although no eye drops had been used. The optic disc was bluish-white, and there was peripapillary edema. On account of the rather frequent association of measles with diphtheria, the case was treated with Roux's anti-diphtheric serum. In all, five injections of 20 cgm. each were given at intervals of four days. Some improvement of vision was noticed by the patient the day after the first injection. The vision steadily improved, reaching normal four weeks after the first dose of serum. She was last seen five months after the occurrence of the amaurosis, when the vision was perfect. Notwithstanding the clinical improvement, however, the appearance of the optic disc remained as at first.

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* Ann. of Ophthal. (January, 1912).

† Anales de Oftalmologia (April, 1913).

The Ocular Symptoms of Scarlatina.—This well-known disease is often followed by various ocular sequels.

The *eyelids* in scarlet fever present a bright-red color, with more or less edema, and a sensation of intense burning. A catarrhal conjunctivitis accompanied by a more or less severe chemosis is sometimes present. The edema is at times so marked that the patient is unable to open the eyes, and the condition is likely to be mistaken for erysipelas. During the stage of desquamation large, thin scales separate from the lids. These should not be removed but mild astringent ointments should be applied. The eyes should be shaded from the light, and the conjunctival infection should be treated with mild boric collyria and simple salves.

Dutoit* reports the case of a boy, aged 16 months, scalded in one eye the day before the eruption of scarlet fever. Violent conjunctivitis occurred, corneal ulcer developed, and ended in total staphyloma. The discharge contained a few staphylococci, and enormous quantities of streptococci. The latter were also present in the nose, and Dutoit supposes that the injured eye became infected from nasal mucus. Bane reports the case of a child two months old, in whom rapid softening and destruction of the cornea occurred with scarlet fever; and the streptococcus was found in the nose and in the eye.

In an epidemic of 2000 cases of scarlet fever with 200 deaths Giuseppi† saw four cases of *corneal ulcer*, two of *iritis*, and four of *panophthalmitis*, which all developed during the course of the disease. One case, with corneal ulcer, was fatal on the twelfth day, another that developed on the eighth day left the patient blind. One eye affected with iritis had to be enucleated. All of the cases of panophthalmitis were fatal and all ran an acute course. Bilateral mydriasis with ocular hyperemia was noted as always followed by death within 48 hours. This was true even of patients who did not appear to be very ill when the mydriasis appeared. Giuseppi suggests that this symptom was caused by a severe toxic action on the adrenals and sympathetic nervous system.

In **chicken-pox or varicella** the skin of the eyelids may be affected; sometimes the disease shows itself first in this region. Römer reported a case of varicella of the lids in a child eight months old. It seems that the conjunctiva is rarely affected by the eruption. Iridochoroiditis and optic neuritis have been observed by Hutchinson, although he did not believe that the intra-ocular disease was the result of the chicken-pox. Steffan has, however, described acute iritis as probably due to the disease.

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* Oph. Year-book (1909), p. 67.

† Gaz. degli Osped. (1918), p. 803.

Vaccinia of the eyes generally shows itself as a vescicular eruption (*vaccine blepharitis*) on the lid margins. This is usually the result of accidental inoculation by some object (finger nail, for example) that has been in contact with a vaccin vescicle or virus. In that case an infective conjunctivitis is sometimes followed by a corneal ulcer.

The **eye symptoms of small=pox** are important because the most serious ocular complication of the disease—*corneal ulcer*—is much more frequent in children than in adults. Fortunately the practice of vaccination is almost universal in America and we consequently now see few cases of ophthalmic variola.

According to Parsons* small-pox was a frequent cause of blindness (1.3 to 2.5 per cent.) before the introduction of vaccination. Hirschberg calculates it to have been as high as 8 per cent. Intra-uterine infection from the mother may cause phthisis bulbi. From 38 to 78 per cent. of eye diseases from variola affect the cornea. They generally show themselves from the twelfth to the fourteenth day; never before the tenth day. The eruption on the lids causes edema and secondary cellulitis of the face, which may be followed by distortion of the lids. There is generally infective conjunctivitis, sometimes with marked chemosis or hemorrhage. Pustules may form on the conjunctiva; Adler says in 30 per cent., Hebra in 1 per cent. of the cases. Wagenmann reports a case in which the eruption was confined to the conjunctiva. There has been much discussion as to whether the keratitis is due to pustules; and it is now generally agreed that it is not. Small, circumscribed infiltrations, interstitial keratitis and hypopyon ulcer have been rather frequently observed. Hirschberg has noted neuroparalytic keratitis; Manz and Adler keratomalacia. The severity of the corneal complications is not always proportional to the general disease.

Primary *iritis* occurs in from 13 to 17 per cent., it is generally part of a uveitis with choroiditis and vitreous opacities, and may lead to complicated cataract. Simple plastic iritis and chronic iridocyclitis also occur. Retinal hemorrhages, retinitis, albuminuric retinitis, uremic amaurosis and detached retina have been reported. Optic atrophy, neuroretinitic choked disc, retrobulbar neuritis, glaucoma (hemorrhagic glaucoma in hemorrhagic small-pox), dacryocystitis, lachrymal fistula, dacryoadenitis, periostitis and many other sequelæ are on record.

Small-pox manifests itself on the *eyelids* in the papular, vesicular, and pustular stages. The integument becomes swollen and edematous as well as bright-red in color. A more or less marked conjunctivitis shows itself, and it is sufficiently severe to cause the escape of an appreciable quantity of mucopurulent secretion. The eyelids themselves burn and itch. Efforts to relieve this by rubbing with the fingers may produce inoculation of non-affected parts of the skin and of the conjunctiva. An efficient means of treating the itching is by the use of red rays, which not only alleviate this symptom, but prevent subsequent pitting. In any event, the further development of pus must be arrested. This is to be done by applications and instillations of efficient antiseptics. The eruption, although not commonly severe on the lids, being usually discrete in its distribution, at times is aggregate and even confluent.

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* "Pathology of the eye," p. 1324.

Corneal inflammations and ulcers may develop as an extension from the pustules situated at the limbus, but more frequently they appear independently. The condition may also result from endogenous infection.

The ocular complications of small-pox are reviewed by Del Monte* on the basis of the statistics of Italy. Although the conjunctiva and iris may be affected, only the corneal lesions are of much importance. Exceptionally a pseudomembranous conjunctivitis occurs, which is always followed by death. The corneal complications include small superficial lesions, ulcers with necrotic base, those produced by pyogenic bacteria, and corneal pustules. The corneal complications are more frequent in children. The appearance of a diffuse epithelial clouding, or of deep purulent infection of the cornea, between the end of the eruptive period and the beginning of desiccation, is a sure sign of death. The only lesion of the iris is a mild unilateral iritis that occurs in adults.

The Ocular Sequelæ of Cerebrospinal Meningitis.—Especially in the epidemic form of this fatal disease of infantile life, certain neuro-ophthalmological changes are common. As Hecht† says, when one meets with any form of septic meningitis due to an invasion of the pia by a streptococcus or staphylococcus (the endemic form seen in infants), the tuberculous and syphilitic types or the epidemic cerebrospinal meningitis caused by the diplococcus intra-cellularis of Weichselbaum, we are impressed with the fact that in all forms the pathological process may be sufficiently extensive to implicate the entire convexity of the brain and more commonly the base, inclusive of all the cranial nerves. That being the case, it is not strange that ocular manifestations are at some time conspicuously present in one or all of the varieties of meningitis. In the septic forms the convex pia is a favorite site; in the meningitis of infants the base is more often involved; the tuberculous variety is preponderatingly basilar; likewise the syphilitic type, in which a degenerative neuritis is present involving the more anterior of the cranial nerves at the base, especially the optic and oculomotor. In the epidemic form the pia of both brain and cord is affected.

Consistent with this localization, neuro-ophthalmologic observers assert the possibility in meningitis of (1) pupillary inequalities and irregularities; (2) iridoplegia; (3) strabismus; (4) nystagmus; (5) optic neuritis and atrophy; (6) exophthalmos; (7) hippus; (8) ocular paralyses; (9) keratitis.

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* Ann. di Ott., xi (1912), p. 852; Arch. di Ott., xviii (1912). p. 663.

† Wood's "System of ophth. therapeutics," p. 293.

According to Uhthoff, metastatic ophthalmia occurs in 4 or 5 per cent. of all cases of cerebrospinal meningitis. It is usually unilateral, but occasionally both eyes are simultaneously affected. It is generally considered that the purulent metastasis commences nearly always in the retina or choroid and involves the uveal tract. Generally there is purulent retinitis with propagation of the inflammation to the vitreous and iris. Lesions of the optic nerve or of its sheaths have not often been found. Meningococci have been found in the blood of patients affected with metastatic ophthalmia, which tends to show that the metastasis occurs through the circulation. They have also been discovered in the interior of the eye, but only in the commencement of the disease, and have disappeared when the vitreous has been examined a little later, which shows that the metastatic ophthalmia is produced by toxins.

McKee* saw seven cases of epidemic cerebrospinal meningitis in which ocular complications were present. One was a case of metastatic ophthalmia and six were cases of conjunctivitis. From the pus in the anterior chamber of an hypopion iritis and from the conjunctiva in two cases of conjunctivitis were cultivated Gram-negative diplococci, which were carefully studied and shown to be meningococci. To these cases is to be added the cultivation of the meningococcus once from the normal conjunctival sac. The author lays stress upon the inaccuracy of basing a diagnosis of the meningococcus upon the presence in smear preparations of Gram-negative diplococci. Meningococci can only be positively demonstrated by carefully studying them in cultures on various media.

The *treatment* of the eye symptoms is of course involved in the conduct of the cerebrospinal disease with which they are so intimately associated.

The **ocular sequels of typhoid fever,** in addition to the serious optic neuritis discussed above, are corneal ulcer, infectious iritis, paresis of accommodation, orbital cellulitis and tenonitis, all of which are fortunately rare.

The **ocular complications of diphtheria** include the infection and implantation on the conjunctiva of the Löffler bacillus, usually in company of other harmful organisms. In this serious form of *membranous conjunctivitis* it appears that the presence or absence of the Klebs-Löffler bacillus cannot be relied upon in the differential diagnosis of diphtheria, for, as the investigations of Morax and others have shown, it has been found in cases which clinically fall in the croupous group; and its presence has not been demonstrated in severe cases which have all the characteristics of diphtheria, as has been shown by Weeks, Standish, and Burnett. The only microbe found in these cases was a streptococcus. At the present time the views of Coppez, who finds that the symptoms, both local and general, gradually merge in the two affections, are accepted. Some cases diagnosed as croupous conjunctivitis have been followed by fatal systemic infection, and others by post-diphtheritic paralysis. Gossetti and Iona found the diphtheria bacillus present in 6 out of 29 cases of croupous conjunctivitis.

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* Ophthalmic Record (September, 1908).

Until the extended use of diphtheria antitoxin true diphtheria was one of the most common causes of serious eye diseases. As it affects the external eye the disease may be divided into three stages: Those of infiltration, suppuration, and cicatrization. In the first stage, which lasts from 6 to 10 days, the symptoms are similar to those attending purulent ophthalmia; the pain is, however, much more severe in the diphtheritic form. The lids are not only swollen and painful, but hard, feeling, sometimes, like board, and it is not possible to evert them. The conjunctiva of the lids is thickened and infiltrated with a plastic material, which may in severe cases extend to the bulbar conjunctiva. If this is stripped off, the surface beneath is of a gray or buff color, the same as that of the layer of the infiltrate, and not red and bleeding, as in croupous conjunctivitis. Ecchymoses are quite commonly seen in the substance of the conjunctiva, which is not already infiltrated. There is danger at any time during this period of corneal necrosis from pressure on the vessels by the exudate, and this destructive process may advance so rapidly that the eye may be destroyed in 24 hours. The discharge is at first watery and flocculent, resembling that of a beginning purulent inflammation. The next stage is marked by an amelioration of the acute symptoms, a diminution in the hardness of the lids, and a change in the discharge to a more purulent character. The membrane begins to disappear by absorption, and is not cast off in patches, as in the croupous form. The conjunctiva begins to look reddish, raw, and succulent, and it is from this source that the purulent secretion now flows. In severe cases, however, the patches slough out, leaving defects in the conjunctival substance which heal by cicatrization. This constitutes the third stage, in which the conjunctiva is left atrophic and shrunken, when symblepharon and even exophthalmos may be produced. Involvement of the cornea, a frequent complication, assumes the form either of local ulceraton or of diffuse infiltration. The advent of corneal involvement is followed by severe pain.

It is no uncommon thing for relapses to occur, and this should always be guarded against as far as possible by careful attention to the local and general conditions.

In every marked case of diphtheritic conjunctivitis there is always more or less systemic disturbance; the depression of the vital forces is sometimes as profound as in the exaggerated forms of faucial diphtheria. There exists frequently a concomitant or subsequent conjunctival, faucial, and nasal diphtheria.

The discharge is contagious and the same precautions as to infection should be observed as are applicable to purulent conjunctivitis. It attacks by preference the young and it seems probable that the contagion can be conveyed by the air and that its direct transference is not necessary for infection. Generally both eyes are involved.

As the chief etiological factor is the Klebs-Löffler bacillus, an absolute diagnosis is impossible without a bacteriological examination. Coppez states that there is a group of bacteria—the xerosis bacillus, the pseudo-diphtheria bacillus of Hoffmann, and the bacterium septatum of Gelpke—which can be distinguished from the true diphtheria bacillus only by culture or by inoculation experiments. To make certain of the diagnosis of ocular diphtheria, he advises examination of cover-glass preparations, cultures on serum-agar, and the use of the Ernest-Neisser double coloration. Owing to the uniform presence of the xerosis bacillus on the conjunctiva, a microscopic examination of the ocular discharge is less valuable than in faucial diphtheria.

In the *treatment of diphtheritic conjunctivitis* general sustaining, and even stimulating measures, are called for if the vital depression is at all marked. As soon as a positive diagnosis of diphtheritic conjunctivitis has been made, an injection of antitoxin must be given. The earlier this is done the less will be the danger of corneal sloughing. The injection should be repeated at the end of 24 hours. Improvement is generally noticeable at the end of a few hours. Locally, cleanliness, with mild antiseptic or aseptic solutions and cocain, is indicated, but in carrying out these measures we are much hampered by the fact that the lids are so hard and unyielding as to make eversion and sometimes even separation impossible, and it should not be attempted in any forcible manner, on account of the intense pain and probable aggravation of the condition it produces. The local application of hot water should be employed frequently and for a longer time than in the croupous form of the disease, as it alleviates pain and hastens resolution. The application of cold, especially if continuous, is likely to diminish still further the vitality of the parts, already much impaired. It is not advisable, unless urgently indicated, to make a canthotomy for the relief of pressure, on account of the danger of opening up a new avenue of infection for the diphtheritic inflammation, and thus adding to the complications of the disease. When the stage of purulency has arrived, nitrate of silver is the remedy, but it must be used cautiously in the beginning, as the application of strong solutions has been followed by exacerbation of the symptoms and a reformation of the membrane. Formalin, in solutions varying in strength from 1 to 2000 to 1 to 500, according to the degree of purulency, has been recommended. Many topical remedies have from time to time been suggested and tried, to assist in the resolution of the exudation, such as citric acid, powdered quinin sulphate, etc., but none of them has had general acceptance in the therapeutics of the disease. The internal administration of mercury has been recommended by good authorities: Five to ten centigrammes of calomel, given every two hours until visible effects of bringing about absorption of the exudation are manifest. This may be assisted by inunction of mercurial ointment.

If the cornea becomes ulcerated, atropin should be used in connection with hot applications. Cauterization of the ulcers should not usually be attempted in the first stages, since they are usually due to lowered vitality and not altogether to microbic infection. Later, however, when resolution is setting in and vitality has returned, cauterization with the actual cautery or with formalin 1 to 60 is useful.

During the stage of cicatrization care should be taken to prevent adhesions between the lids and the ball, which is likely to take place when the two raw surfaces are brought together. The lids should be moved frequently over the ball, and vaselin used freely as a protection to the raw surfaces. It may be necessary to introduce a bit of thin charpie between them to keep the raw surfaces apart. The sound eye should be protected by a Buller shield.

The effect of the toxins of diphtheria upon the *extrinsic ocular muscles* and upon the *accommodation* is well known. The *pareses* so produced are generally temporary, both the cycloplegia, heterotropia and heterophoria usually disappear within a few weeks after the first recovery of the patient from the systemic poisoning. Sometimes, however, the paralysis persists.

The account given by Story* of the effect of diphtheritic poison upon the ocular apparatus is a useful contribution to a study of the whole subject. He says that in *post-diphtheritic paralysis* of accommodation there is a positive increase of hypermetropia, *i.e.*, during the paralysis the hypermetropia is greater than can be rendered manifest subsequently by complete atropinization. Jacobson† has accounted for this by the supposition that the crystalline lens may assume a flatter curvature in long-continued paralysis of the ciliary muscle than it does in the briefer paralysis induced by atropinization. The effects of long-continued atropinization in myopic children support this explanation; but, as Förster observes, the existence of a certain range of accommodation in most of the diphtheritic cases is a fact which tells the other way. Regular astigmatism has also been observed to be present during the diphtheritic cycloplegia, and has been accounted for by the theory of a dynamic lenticular astigmatism, as held by Dobrowolsky and Woinow, which ceases to assert itself during the presence of the paralysis. The lesion of accommodation shows itself at various times, but usually from the third to the sixth week after the commencement of the throat affection. It generally passes off after a few weeks, but may persist for months. Eserine appears to have some influence in shortening its duration. The acuity of vision also may suffer, probably not from any lesion of the optic nerve or retina, but possibly from a lenticular astigmatism due to the same cause as the abnormal hypermetropia. The paralysis of accommodation comes on rapidly, and occasionally suddenly. It lasts for weeks or months, and gradually disappears. Most cases seem to occur in from four to six weeks after the onset of the diphtheritis, or in from two to three weeks after its subsidence, and the great majority of patients have been young subjects. The lesion is observed after the mildest and most insignificant attacks as well as after the most severe. It has been stated that retinal hyperemia is present in some instances, but the vast majority of observers have found the fundus perfectly normal. It is not necessary to have the pharynx affected in order to induce post-diphtheritic ocular paralysis. Diphtheritic inflammation elsewhere is equally potent. Scheby-Buch has collected cases of diphtheritic inflammation in various parts of the body which were followed by paralysis, and in which no pharyngeal diphtheritis was present.

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*"System of diseases of the eye," iv, p. 700.

† Archiv. f. Ophth., xii, p. 47.

Ptosis has been observed occasionally, and strabismus pretty frequently. Paralysis of both recti interni or of both externi has been recorded. The external rectus seems peculiarly liable to be affected. Remak* found abducens paresis in 10 cases out of 100 post-diphtheritic ocular lesions. It is possible that the phenomenon in some of the cases of the latter group may be accounted for by spasm of convergence. Complete ophthalmoplegia externa has also been observed.

Garcia del Mazo† records the occurrence of *retrobulbar optic neuritis* with paresis of the sixth cranial pair following diphtheria in a girl of nine years. Prompt recovery from severe diphtheria followed the use of serum. Early paralysis of the velum palati occurred. Indistinct vision was complained of several weeks later. The visual field was also contracted. Two weeks later both externi were paralyzed. Complete recovery followed.

These eye symptoms are, of course, involved in the general therapy.

Ocular Symptoms of Chorea.—Prominent among the signs of St. Vitus' dance in children is *blepharospasm*, which sometimes precedes and acts as a danger signal of a general attack. Errors of refraction and muscular defects are said by some to be one of the causes of chorea, and cases of cure of the disease from the wearing of correcting lenses have been reported. In general, the eye muscles are not involved in the choreic movements; only in rare cases do we find unrest or spasm in solitary extrinsic muscles. When present these have the typical, clonic, rapid character of chorea, and may even produce temporary squint with diplopia. In addition, spasm may occur in the orbicularis palpebrarum, manifesting itself as nictitation; sometimes as a more decided blepharospasm. In a word, cramp of the eye muscles in chorea behaves quite like cramp of other muscles.

Much more serious are those instances of *embolism of the central artery of the retina*‡ and *optic neuro-retinitis* that have been published on the best authority. It must be remembered that in many cases of chorea there is also present some form of acute rheumatism with its cardiac and other complications; and these ocular conditions may be due to the vascular changes rather than to the chorea proper.

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* Centralbl. f. prakt. Augenheilk. (1886), p. 161.

† Arch. de Oft., xiii (1912), p. 354.

‡ Gowers, Royal Lond. Ophthal. Hosp. Reports, viii, p. 181.

Ocular Relations of Diabetes in Childhood.—Most of the organic lesions and many of the ocular signs and symptoms of the much less serious adult diabetes have been found in the grave forms of glycosuria in children. However, differences in tissue disposition and the fact that the so-called juvenile diabetes generally runs a comparatively short course to a fatal termination and does not permit the development of those chronic changes in the ocular vessels and other parts of the youthful eye so often seen in the adult. The most important of the eye diseases that accompany the presence of glucose in the blood and tissues of the body are *cataract, iritis, retrobulbar neuritis, oculomuscular pareses, optic neuritis* (sometimes followed by atrophy) *accommodative failure, changes in the refraction, retinitis, retinal hemorrhage* and *lipemia retinalis.*

Grandclement* states that 30 youthful patients in whom he saw patches of *retinal hemorrhage* all died within 15 to 18 months.

Retinal limpemia has been observed only in severe diabetes and usually near the fatal termination of the disease. Instructive cases are reported by Köllner† and Darling‡ making in all eight cases now on record. Köllner's patient was passing 12 liters of urine daily, containing 2 to 6 per cent. of sugar. The retinal vessels were flesh-colored, and as they approached the periphery became pure white. It was impossible to tell the arteries from the veins. They were all dilated, but presented no other pathological changes, and the retinas were otherwise normal. The blood was found to contain 26.25 per cent. of fatty matter that could be extracted with ether, and 2.16 per cent. of cholesterin. The choroidal vessels were normal in color. Köllner points out that the oldest patient presenting this condition, so far reported, was 28 years of age.

In two cases of diabetes mellitus associated with *optic nerve involvement* Hoffmann§ found glycogen in the axis cylinder and sheaths of the nerve, associated with marked changes in the medullary sheaths. In one case lipemia was demonstrable by microchemic tests.

H. Gifford|| urges care in the *prognosis and treatment* of *juvenile diabetic cataract.* In this form of the disease the lens opacity often develops rapidly in a week or two. He found inflammatory complications in these cases very frequent, his own failures amounting to 43 per cent. He urges the importance of examination of the urine in all cases of cataract, even when there is a history of traumatism. His conclusions are as follows: (1) No diabetic cataract shold be operated on without letting the patient or the relatives understand that even if a good result is obtained the patient will probably not live more than a year or so to enjoy it. (2) That the risk of a bad result is much greater than in ordinary cataract, and it involves some danger to

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* Lyon Med. (Jan. 16, 1910).

† Zeit. f. Augenheilk., xxvii (1911), p. 411; Ophthalmoscope, x (1911), p. 535.

‡ Arch. of Ophth., xl (1911), p. 355.

§ Munch. med. Wochenschr., No. 47 (1912).

|| Ophthalmic Record (May, 1911).

the patient's life. (3) That if a good result has been obtained in one eye it is unjustifiable to operate on the other eye.

Cazalas* states that *diabetic iritis* is a rare affection. The cases of iritis from other causes appearing in a diabetic are much more numerous. In either case, the diabetes renders the patient more subject to attacks of glaucoma. Therefore in combating the iritis, the use of atropin must be guarded. The patient should be kept under the most careful observation, and at the first signs of hypertension the atropin must be replaced by eserin.

Zentmayer† reviews several of the hypotheses which have been advanced to explain the *decrease* which occasionally occurs *in the static refraction* in diabetes. He reports a case in which the hyperopia of each eye increased about 2 D. with a development of low astigmatism against the rule. The acquired hyperopia was manifestly greater than could be due to simple paresis of the accommodation. The increase of hyperopia coincided with a lessening of the percentage of sugar in the urine. At the end of a year and a quarter the hyperopia had diminished by about 1.5 D. in each eye. The presence of a transitory astigmatism against the rule is in favor of a lenticular change.

The *treatment* of the ocular disorders of juvenile diabetes is closely bound up with the conduct of the underlying glycosuria (described elsewhere in this work) and the grave prognosis usually given in the one has its counterpart in the forlorn hope of the visual complications. There is, moreover, little or nothing to add to the *topical treatment* indicated in the corresponding adult affections. When an exception to this rule occurs it will be noted under appropriate headings in this chapter. See, for example, *Cataract* under "Diseases of the Lens," and *Iritis* under "Diseases of the Iris."

Eye Signs of Anemia and Chlorosis in Children.—These manifestations of diseases are deliberately though empirically listed together in view of the fact that, as in *albuminuria*, pretty definite ocular manifestations accompany them *as such* whatever be the actual or varying characters of the pathologic entities of which they are a part.

It has long been noted that the *photophobia* and irritability often observed in the eyes of chlorotics are usually traceable to conjunctivitis and blepharitis, and these again may result from overtaxing a weakened accommodation, which often leads to hyperemia of both the external and internal eye.

The (usually) harmless swelling of the eyelids in this disease calls, however, for a careful urine analysis in order to detect a possible nephritis.

In chlorosis a rapid *increase of myopia*, or *decrease of hypermetropia*, is not uncommon and is probably due to diminished resistance of the sclera. Moreover, opacity of the vitreous and the inflammatory changes at the posterior pole are observed in cases of chlorosis which are absent in the common form of progressive myopia.

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* Thése de Toulouse (1910); abst. in Rev. Gen. d'Ophtal., xxx (1911), p. 358.

† Sec. on Ophth., A. M. A. (1911), p. 280; Journ. Am. Med. Assn. (Aug. 5, 1911), p. 470.

Anemia and chlorosis have been described by some as the cause of all kinds of disease of the eye but it seems clear that in many of these reported cases they are dependent upon incidental complications. Thus, *iritis*, *scleritis*, *iritis serosa*, and *opacities of the vitreous* accompanying forms of uveitis posterior have been attributed to these constitutional diseases.

Relapsing vitreous hemorrhages in young individuals have also been observed in anemia, and without doubt that condition is responsible.

Optic nerve disorders, especially certain forms of neuritis, are much more certainly and more closely related than are the foregoing. Outside of true *neuritis optica*—the causes of which may be intracranial—only a certain form of papillary congestion occurs. This form of congestion can be traced to a purely edematous process accompanying a hyperemia. Vision may be normal or nearly normal and so continue a long time under these conditions. Occasionally the disc is much swollen, although the elevated papilla appears clear and transparent and has a faint, edematous appearance; in other cases one finds a simple edema. The vessels are but little changed, although the retinal veins may appear darker, enlarged and tortuous. In some cases white opaque bands are seen in the papilla and white plaques have been observed in the retina not unlike those found in albuminuric retinitis. These hyperemic or inflammatory changes may go on to atrophy.

Retrobulbar neuritis in juvenile anemics is analogous to the forms occurring in adult alcohol and nicotine intoxications. These forms, too, may end in partial atrophy.

Malignant *atrophy of the optic nerve*, similar to that following amaurosis from excessive hemorrhage (white discs and narrow arteries) with almost complete blindness in both eyes, has been observed.

The *prognosis* of all chlorotic eye disorders depends upon the character of the primary disorders. Retrobulbar neuritis generally permits a favorable prognosis even if a partial degeneration of the optic nerve has taken place, and the same observation holds good of a papillitis edematous in character. A favorable outcome may also follow those forms of papillitis which are caused by hemorrhages into the sheath or the trunk of the optic nerve. In the *juvenile form of relapsing hemorrhages into the vitreous humor* the prognosis is decidedly unfavorable.

Ocular Symptoms in Hydrocephalus.—The ocular symptoms of this disease result from pressure on the optic chiasma by the distended third ventricle. They are bitemporal hemi-anopsia, optic neuritis, and optic-nerve atrophy, the latter being secondary or primary according to the severity of the attack. Strabismus is not uncommon.

In one case occurring in a young girl, who complained of headaches, impairment of vision and diplopia, Haben* found paresis of the left adducens, bilateral papillitis (with an elevation of 6 D., *i.e.*, 2 mm.); V. almost ½; pupils from 3.25 to 3.5 mm.; nystagmus in extreme lateral fixation; tremor of head and hands. The patient had always had headaches, but more intensely during the last six months, in which period she had vomiting (lasting one to two days) three times. She was well-nourished, and there was no indication of lues, tuberculosis or spinal disease. The author made the diagnosis of chronic hydrocephalus of the fourth ventricle. As two punctures of the right lateral ventricle transiently reduced the papillitic swelling to 3 D. and relieved the headaches, the operation for permanent drainage of the ventricle was performed. After reflecting a skin-bone flap of the parietal bone, about 2 cm. from the longitudinal sinus, a trocar, 2 mm. wide, was introduced into the right lateral ventricle. At a depth of 5.6 cm. a stream of liquor spurted out. The trocar was replaced by a specially prepared and hardened calf's artery, which connected the ventricle with the epidural and subdural spaces, the wound was sutured and the skull at this region fenestrated. Four weeks later all symptoms had disappeared, the discs were scarcely prominent, although they exhibited a dirty, slightly reddish-gray color, with somewhat indistinct borders. The lumen of the vessels was almost normal; vision was normal.

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* Practical Med. Series, Eye (1910), p. 212.

Ocular Relations of Infantile Paralysis.—There are few or no eye symptoms significant of this disease, although optic neuritis, hemi-anopsia, paralysis of the ocular muscles, and, occasionally, nystagmus have been noted. Cases with optic atrophy associated with diplegia have been reported by Freund.

In a child 6½ years old, Sachs saw papillitis, blindness, left ptosis, sixth nerve paralysis, right corneal anesthesia, and right spastic hemiplegia with a hemorrhagic cyst in the left temporosphenoidal lobe which pressed on the left crus cerebri.

Amaurotic Family Idiocy.—The eye symptoms in the so-called Tay-Sachs disease are significant and fairly constant.

The optic discs in the early stages are healthy. The characteristic fundus lesion lies in the region of the macula lutea of each eye, where this is seen as a large white area, tolerably diffuse, with softened edges, covering a space about twice the size of the optic papilla. At its center is a brownish-red, fairly circular spot, contrasting strongly with the white patch surrounding it. At a later period, along with complete blindness, there is atrophy of the optic nerve.

R. M. Smith* has reported two cases occurring, as usual, in Hebrews. The characteristic symptoms were a mahogany-red spot on a white or grayish background in the macular region, decreasing vision, progressive paralysis, mental deficiency going on to idiocy, nystagmus and drooling. All died before three years of age.

H. B. Sheffield† has recorded the case of a Hebrew child of 11 months. It developed well the first six months; then the infant gradually became pale, flabby, less active physically and mentally, and developed the characteristic fundus changes above detailed, with blindness and idiocy. The child died of pneumonia. An older brother and sister were normal.

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* Boston Med. and Surg. Jour. (Mar. 7, 1912), p. 370.

† N. Y. Med. Record (Jan. 27, 1912), p. 165.

H. Gifford* states that as opposed to the Tay-Sachs, or infantile form of family amaurotic idiocy, which begins in early infancy and almost invariably leads to death before the fourth year, Vogt pointed out in 1905 that there is a juvenile form beginning, not in infancy, but in early youth; leading slowly to blindness, frequently with paralysis, death after several years, and showing no predilection for the Jewish race. Gifford reports two children affected at seven years, out of seven living children of mentally defective parents; and also mentions a group of five children which he thinks probably belongs on the outskirts of this group, though decidedly atypical.

V. Magnus† has reported a boy of seven with defective sight, motor disorders and optic atrophy, whose sister had died at 14 after suffering blindness, paralysis and dementia. He also reported a case resembling typical amaurotic family idiocy of the infantile type occurring in a family of seven children, the other six being healthy. The parents were of old Norwegian peasant origin, without admixture of Jewish blood, were not related, and no nervous or mental disease had affected their families so far as their knowledge went.

Ochi‡ reports a typical case of Tay-Sachs disease, the first reported from Japan. He made a microscopic study of the eye-ball, and found the usual degeneration of the ganglion cell layer and atrophy of the nerve fiber layer.

A. Hymanson§ reports six cases of Tay-Sachs disease. In the first two cases studies in metabolism showed that it was not disturbed. A complete post-mortem examination of one of these cases was made, with microscopic findings. The next two cases were unique in that two brothers were married to sisters, and *their* parents were first cousins. Several of their children were afflicted with amaurotic family idiocy. In the last two cases the disease affected twins. Death occurred between 17 and 24 months in each case; and all were of Jewish parentage. Hymanson stated that while the infantile form is usually seen among Hebrews, the juvenile type of the disease is far more common among Gentiles. He expresses the opinion that it is the duty of every physician to discourage the marriage of near kin, and also of persons in whose family there is a neuropathic taint.

Cranial Deformities and Their Ocular Symptoms.—As is pointed out elsewhere in this work, the principal types of this class of cranial deformity are *tower-skull* and *oxycephaly*, conditions resulting from premature union of the coronal suture. In the latter disease the cranial dome is insufficiently elevated and lateral extension takes place below; the temporal regions bulge and the zygomata protrude. Other structural changes also occur, so that the orbital space is diminished in varying degrees, influencing the amount and character of the *exophthalmos*. Some of the cases are undoubtedly hereditary. Deformity of the optic foramen and possibly pressure upon the nerve are responsible for the optic neuritis and the post-neuritic or primary optic atrophy.

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* Ophthalmic Record (November, 1912), p. 511.

† Norsk. Mag. f. Laegevidensk., lxxiii, p. 1598.

‡ Nippon Gank. Zasshi (November, 1912).

§ Archives of Pediatrics, xxx (November, 1913), p. 825.

Michael Goldenburg[*] discusses especially the *etiology* of *tower-skull* in respect of the eye symptoms. He finds that it is quite probable that malformations of the head are more commonly the cause of eye lesions than one is led to believe. To 1912 only 26 cases of tower-head with ocular lesions had been reported. Enslin,[†] who looked for these cases over a period of two years, out of 9380 eye patients found 16 cases of this kind.

Tower-skull, *per se*, as a cause of eye disease, is still problematic, for we find a number of cases reported of this shaped head without any eye lesions at the time of examination.

In the 42 cases reported to date, 36 had post-neuritis atrophy, 2 double neuro-retinitis, 2 one-sided papillitis and post-neurotic atrophy, and 2 cases primary optic atrophy.

The question arises whether the tower-skull is the direct or indirect cause of the optic nerve lesion. The theory propounded, that the causal factor responsible for the malformation of the skull is also the cause of the optic nerve lesion, has a number of adherents.

That a prenatal osteitis is present, and is the probable cause of the premature ossification of the sutures, nearly every one is agreed upon. The etiology of osteitis, at least in adult life, is infection of some character. That a metastatic infection during intra-uterine life is possible there is no doubt and is not strange to ophthalmology.

Enslin discovered six specimens of tower-skull with papillitis but could not demonstrate in them constriction of the optic foramina; he, however, states that this does not entirely detract from the compression theory, as the skulls he examined were old and very dry.

The factor of *hydrocephalus*, internal or external, as the cause of the eye lesion, *per se*, is of considerable importance. Whether this is a transitory form, as suggesed by Friedenwald.[‡] or the result of premature ossification of the sutures remains an open question.

In Goldenburg's patient the eyes were very prominent and the child did not seem to show evidence of being able to see very much, as far as the mother can remember. The child's well-marked *tower-skull* had a bi-temporal circumference of 17¾ in.; a sagittal measurement of 14¾ in. from nasion to occipital protuberance; perpendicular from nasion to highest point of the skull of 5½ in. and an anterior-posterior diameter of 5½ in. The eye-balls were very large and the sclera thin; the cornea normal in size, transparency, and sheen; a divergent strabismus with a marked horizontal nystagmus; anterior chamber and iris negative. The pupillary opening was about 6 mm. and equal in both eyes; the pupils reacted very sluggishly to bright light. Tension negative; vision in R. eye = 0. Discs a dirty-gray, and outlines not well defined; there was an uncertainty as to the caliber of the vessels, owing to the marked nystagmus, but the writer was inclined to think that there was some evidence of a perivasculitis. Direct ophthalmoscopy was very difficult and unsatisfactory. Roentgenographs showed the skull to be very irregular in thickness with numerous depressions on the inner table undoubtedly formed by the convolutions of the brain. Suture lines were not demonstrable; and the grooves of the meningeal vessels or diploic veins were markedly accentuated. The sella turcica was approximately normal in size. No evidence of changes responsible for the exophthalmos were discovered.

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[*] Am. Journ. of Ophthalm. (November, 1918).

[†] Virchow's Archiv., lviii (1910).

[‡] Archives of Ophthalm. (1901).

Meningitis and Its Eye Symptoms.—All varieties of meningitis, both of the erebral base and convexity, as well as of the spine, are apt to be associcted with *optic neuritis.* The ocular signs of the infantile *epidemic cerabrospinal* form have already been discussed.

In *acute teubercular meningitis* there are found, in from 15 to 70 per cent. of the cases, miliary tubercles in the choroid. These tubercles appear as round, slightly elevated, pale-yellowish spots, with undefined edges, varying in size from 0.5 to 2.5 mm., situated in the neighborhood of the optic nerve and the macula lutea. It has been demonstrated, on examination after death, that many more tubercles are present than were discovered during life.

Miliary tubercles in the choroid also appear in cases of *general, acute miliary tuberculosis* when meningitis is not present.

Optic neuritis is more common in this than in any other form of meningitis.

Both in the sporadic and in the epidemic forms of *cerebrospinal meningitis* eye symptoms of various kinds are extremely common. Retinitis and plastic irido-choroiditis with purulent infiltrations of the vitreous, which may at times go on to panophthalmitis, are often seen. Ophthalmoscopic examination reveals optic neuritis or neuro-retinitis or, perhaps, only congestion of the optic disc and engorgement of the retinal veins. The optic neuritis of this disease is liable to end in atrophy of the nerve.

Traumatic meningitis, due to falls and blows on the head, without fracture of the skull, is sometimes also followed by optic neuritis, which may lead to optic atrophy. In some cases of hemorrhagic pachymeningitis optic neuritis or congestion of the papilla has been seen.

Optic neuritis is rare in uncomplicated *otitic, purulent meningitis* but typical choked disc in purulent otitis or mastoid disease is probably always an expression of grave intracranial complications (cerebral abscess, subdural abscess, sinus thrombosis, etc.).

Eye Symptoms of Dementia Præcox.—The chief study of the ocular complications of this disease are by Tyson and Clark* who give the results of their examination of 115 consecutive cases. They found definite changes and symptoms in all genuine cases of this psychosis. The fundus changes, as seen clinically, are divided by them into three groups, which are usually in the order of their occurrence as follows: (1) Congestion of discs, hyperemia and edema, dilated dark-colored veins, slightly contracted arteries and blurring of the edges of the discs. (2) Congestion of the nasal side, with temporal pallor of the discs, dilated veins, contracted arteries. (3) Pallor of the discs, dilated veins, contracted arteries. These changes constitute anemia and partial atrophy of the optic nerve. All the different forms of dementia præcox were met with, and, while the results by form-types have not been fully analyzed, the authors state that the more marked changes in the eye syndrome were found in the more rapidly deteriorating types of the disease. Coincident with the study of the changes in the papillæ the pupils were examined in 85 cases. The average size of the pupils was about 5 mm. as compared with rather under 4 mm. of the healthy controls. The light reaction was active in 71 cases and sluggish in 14. Consensual reaction was active in 68 cases and sluggish in 17. Accommodation and convergence reaction were active in 71 cases and sluggish in 13. Hippus was present in one case. The sensory pupil reflex was slightly positive in six cases and negative in 79 cases. Pilz-Westphal reaction was positive in two and negative in 85 cases. Corneal sensibility was diminished in 69 cases and normal in 17.

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*Archives of Ophthal., xli, (May, 1912), p. 223.

The visual color fields were examined in 81 cases. All were found concentrically contracted. The authors sum up as follows: The changes in the discs, pupils, visual fields, and corneal sensibility which, when taken together, constitute the new syndrome, are all in accord with each other. In their examination of all other types of insanity, imbecility or idiocy they found no other condition similar to the ocular signs outlined here for dementia præcox. They also consider that the eye symptoms have a prognostic value, as the severer grade of eye changes are found in the more rapidly deteriorating cases.

The *pupillary disturbances* in this disease have been further studied by a number of observers. From a consideration of his own experience of over 200 cases, and of the views of other writers, Bumke arrives at the following conclusions: The average size of the pupils in cases of dementia præcox is larger than the normal; and the diameter of such pupils changes with abnormal frequency and rapidity. In rare cases of catatonic stupor a catatonic rigidity of the pupil is observed, combined with mydriasis or miosis or with various changes of pupillary shape. The pupillary anomaly which is pathognomonic of dementia præcox is the absence of pupillary mobility, of psychic reflex, and of reflex dilation to sensory stimulation, with retained light reaction. This symptom once developed is constantly present, at the height of the disease is found in more than half of all cases, and is almost never lacking in deeply demented patients. It is practically never present in mania, depressive insanity, or in functional psychoses, but is found in other dementias due to cerebral changes. Weiler and Pförtner* call attention to the significance of the same symptom-group. In four cases of dementia præcox Meyer† produced pupillary dilatation by pressure on the iliac point: The light reflex was absent so long as pressure was maintained, and reappeared when the pressure was withdrawn.

Infantile Ataxia.—By this title the so-called Friedreich's disease is noted. The *ocular complications* have been studied by several observers. Darier‡ has observed five cases of this rare malady carried over a period of 25 years. The affection begins in early youth and is in general insidious and progressive, but in some recorded cases the onset has been sudden. In some cases no ophthalmoscopic change is found at the start while in others the fundus lesion makes its appearance before the vision is affected. In all instances central vision is affected. Both eyes are in general simultaneously and equally affected, but the rate of diminution of vision varies considerably. In the majority of cases the lesions have been confined to the macula, but in exceptional cases (three of Stargardt and two of Darier) lesions have also been found in the neighborhood of the papilla and in the periphery of the retina. It is obvious that as far as the eye changes are concerned these cases are similar to the amaurotic family idiot type, and Darier proposes to differentiate two types, *i.e.*, familial macular degeneration with it without idiocy. He inclines to the view that the earlier in life the macula is affected the greater the chance of the cerebral functions being also attacked. How and why the lesions appear there is no evidence to show. Syphilis can be excluded.

The author's new patients come from two separate families. In the first group two out of four surviving children were affected, both females. In the second group there were three affected out of seven, and these were all males. In two of these the lesions had extended considerably beyond the maculæ.

Whooping-cough. Pertussis.—The paroxysmal cough of this disease is responsible for *subconjunctival hemorrhages* and, in the opinion and experience of the writer, for many more *retinal bleedings* than are discovered by the family physician. When the latter occurs it either produces no permanent damage and the minute blood clots are soon absorbed, leaving little or no trace, or if visual defects result the child is too young to notice or report it. Bearing on this subject Roedelius§ records a case of *optic atrophy* in a child who died a few weeks after having had whooping-cough. All other possible causes could be excluded. Roedelius was able to find the reports of six other cases, one recovering spontaneously and another after spinal puncture.

CARE OF SCHOOL CHILDREN'S EYES

Ocular Hygiene of Infants.—As the writer of this chapter has often said, it seems hardly necessary in this day and generation to point out that it is quite as important to conserve the eyesight as to restore it. The application of those hygienic rules that have been formulated as the result of a study of ophthalmology is as necessary in the practice of the physician as regulating the dietary or any habit of his patient. Moreover, the family doctor will be constantly called upon to answer such questions as "What is the best light to use in reading?" "What do you think about the type of *this* school book?" "Would you advise us to send John to the kindergarten?"—all of which demand at least some acquaintance with ocular hygiene. It frequently happens, also, that the physician is elected to serve as school trustee or as a member of some school board; how can he intelligently fill such an office unless he is acquainted with the requirements of modern schoolrooms, with all their details of lighting, seating, painting, etc.?—matters of vital moment when one considers that the eyes are the organs chiefly employed and involved in acquiring an education.

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* Zeitschr. f. Augenheilk., xxiv (1909), p. 544.

† Berl. Klin. Woch., xlvii, No. 40 (1909).

‡ La Clinique Ophtalmol. (Jan. 10, 1914).

§ Archiv. für Kinderheilk., lxii, No. 3.

Infants' and children's eyes should never be exposed, even in sleep, to the glare of strong light, artificial or natural, and this is particularly imperative when the child is taken out in a perambulator or carriage. The eyes should then be protected by an awning or parasol lined with material that will not reflect the sun's rays upon the face. They should not be encouraged to use their tender eyes for near work and their playthings ought to be large objects, easily seen. Kindergarten and primary schools recognize this rule, so that the occupations of the child do not injure the eyesight. No fine, difficult, or prolonged visual labor should be allowed lest immediate eyestrain be produced or the foundation for a later myopia be laid. Sewing, mapmaking, perforated card problems, much reading, intricate drawing *et hoc genus omne* should be banished from every primary school. As Pyle properly observes: "If a child has red eyes, holds its book close, complains of not being able to see at a distance, looks at objects sideways or between partially closed lids, or squints or complains of headache, browache, or pain in the eyes, it is the parents' or teacher's duty to send it to a competent oculist. If the oculist decides that glasses are necessary, they should be put on at once in spite of any foolish prejudice, for they will save and promote the physical and intellectual development of the child and prevent many years of suffering and perhaps irreparable ocular disease."

The so-called "stupid" child is too frequently one who has defective eyesight, and in consequence appears inattentive to his studies; the adjective quoted might with great justice be applied to his guardians.

The age at which a child should be sent to school depends largely upon the condition of his visual apparatus. If he has no ocular defects, is otherwise in good health and is never "crammed" or made to study out of schools hours, half a day's schooling may be commenced at seven or eight years of age by the average child. The amount of work may be gradually increased until at 10 he does a full days' work.

Children in poor health, especially if they exhibit ocular or aural defects or show a tendency to myopia, or present evidences of eye-strain, should have little or no systematic schooling before they are 12 years old. That child will be happier and a better citizen, as well as a more successful man of affairs, who develops into a fairly healthy, though imperfectly schooled, animal at 20 than if he becomes a learned neurasthenic asthenope at the same age.

School Houses.—These should always be located and built with particular regard to the eyesight. Ocular defects are most numerous in poorly lighted, badly drained and improperly ventilated schools. The window-space should be at least 1 sq. ft. to every 5 of floor-space. There should be no obstruction to the entrance of sunlight and the nearest buildings should be at least twice as far away as their heights. Light should fall upon the pupils' desks *from the left and rear*, so that there never is any light thrown directly upon or directly reflected into their faces. In this way no shadows are cast by the hand and arm (of right-handed pupils) upon the writing pad or paper. There should be no annoying cross lights, or windows in front. The top floors are best illuminated from overhead sky lights.

Myles Standish* regards as the essentials of proper illumination of schoolrooms:

1. The walls should be painted a very light color, preferably an exceedingly pale green or buff, so as to diffuse daylight freely, and in the evening reflect a generous proportion of the light which falls upon them. (2) The wooden finish of the room and desks should be light in color. (3) The window shades should be able to exclude direct rays of the sun. (4) Direct illumination is desirable. (5) The lighting stations should be so arranged that no annoying shadows fall on the pupil's desk. (6) The newer forms of incandescent lamps and Zalinsky shades, when properly arranged, can give a candle-foot illumination of 2.5 on each and every desk in the ordinary schoolroom. (7) In most cities the expense of the more desirable electricity, used in the manner above described, is not so much greater than the cost of gas as to be prohibitive.

Even on cloudy days it should be possible to read fine (diamond) print in any part of the schoolroom without the aid of artificial light; indeed, no artificial light is ever used in the ideal schoolroom. A north exposure of the schoolroom is preferable, but light from any direction can, at any time of the year, be regulated by shades and awnings, which are preferably of light colors—gray, buff, green or blue. Risley, our chief American authority on this subject, gives the following dimensions of the ideal schoolroom:

	Feet
Length of room	32
Width of room	24
Height of ceiling	15
Window-space (linear measurement)	24
From floor to window-sills (beveled)	3
Height of windows	11

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* Ophthalmology (October, 1908).

The room accommodates 45 pupils, giving 256 cu. ft. of space to each. The walls and ceilings as well as the woodwork should be of the same softly reflecting colors as the window shades. The desks should be adjusted to the individual needs of the pupil and should be chosen with due regard to his comfort; the restless and uncomfortable pupil works the most mischief. If the seat is too high the child's feet are suspended in mid-air; if the desk is too high the elbows cannot rest without curving his spine out of shape, and the eye is brought too near; if too low he stoops over his work, compresses the veins of his neck, brings on cerebral congestion and becomes, in addition, round shouldered.

Blackboards should be of slate, or painted a dull black, so as not to reflect the light falling on them. Most of us have realized the misery of the child straining his eyes in the attempt to decipher, across the schoolroom, the not too plainly written words or figures on greasy, shiny boards. Of course, blackboards should never be placed between windows.

Regular medical examinations of the school children are urgently needed and preferably are made at the beginning of the school year. These investigations of the ocular and aural functions are easily carried on, so easily that the teachers can be readily instructed by the school physician how to carry them on. The plan advised by Frank Allport is to be commended as the best and most practical. It is fully outlined in the following pages.

Children with defective eyes should be sent to an oculist or ophthalmic dispensary and should not be allowed to re-enter school until they have received proper advice and treatment.

School Books.—These should be easily read and ought to be small enough to be readily handled. For ocular reasons they should not contain smaller type than "10 point" (long primer). The lines should be at least $\frac{1}{10}$ in. apart, they should not contain more than 60 letters nor be more than 4½ in. long, so as not to fatigue the ocular muscles in consequence of undue rotation of the eye-balls. The paper used in books and magazines should not be, as it often is, so highly glazed that it acts as a mirror to reflect the light into the eyes. It is, however, not always possible to accomplish this where "half tone" illustrations are frequently used with the text. The type should be distinct and the printing well done. Bad paper, poor ink, and worse printing are too frequently encountered in our books and newspapers.

EXAMPLES OF SPACING

The conjunctival vessels on the globe are in most cases enlarged but, in the milder types, there is no marked redness of the ocular conjunctiva, the thickening and redness being confined to the conjunctiva of the lids, particularly at the junction of the lids and the eye-ball in the retrotarsal folds. Sometimes there is a slight chemosis present.

Improperly spaced.

The conjunctival vessels on the globe are in most cases enlarged, but, in the the milder types, there is no marked redness of the ocular conjunctiva, the thickening and redness being confined to the conjunctiva of the lids, particularly at the junction of the lids and the eyeball in the retrotarsal folds.

Properly spaced.

There are at least 20,000,000 public-school children in the United States. At least 5,000,000 of these children suffer from eye diseases or defects which seriously impair their school progress. About 12,000,000 suffer from eye, ear, nose or throat diseases or defects, which prevent proper school advancement.

Children who have defective eyes, ears, noses and throats cannot, unless relieved, receive and profit by public-school education. To such children, schoolwork is a pain and a burden. They are always behind their classes, sometimes remaining in one room year after year, an exasperation to the teachers and discouragement to themselves. Unless relieved and rendered fit for study, they are regarded as mentally deficient and morally vicious, become personally disheartened and truant, drift into bad society and associations, commit small and then greater crimes and eventually may enter the criminal classes and become an expense and care to the commonwealth as police-court defendants, and as dwellers in asylums, institutions and prisons.

Education is the greatest enemy of crime, and where education is not possible crime in all its phases is almost sure to raise its ugly head. The war cry against crime should then be "Education," and where education is difficult or impossible owing to physical defects or diseases, immediate steps should be taken to relieve or remove such defects, so that children may be able to receive and profit by education, and thus rear good, valuable and respectable citizens and save millions of money that can then be deflected into desirable channels.

New York City has more than 650,000 public-school children, and 30 per cent. of these children are two years behind their natural grades. Ninety per cent. of this misfortune is due to defective eyes, ears, noses and throats. Cronin found in one school 150 defective, backward children; 137 had infected tonsils and adenoids and 13 had defective eyes. These conditions were all removed and almost all the children became good and tractable pupils. This is a striking illustration of what may be done in other schools.

It must not be supposed that eye tests among school-children are advised merely for the purpose of correcting ocular defects by glasses. Such instances are, indeed, extremely frequent, and many children are retarded in their schoolwork by near-sightedness or by other defects, such as hypermetropia, astigmatism, muscular weakness, etc., which prevent easy and comfortable eye service, and which are usually followed by laziness, neglect of work, discouragement, truancy, and school abandonment. But there are many other ocular conditions which the school tests will disclose, such as the various forms of sore and red eyes, iritis, ulcers, cataracts, cross-eyes, and tear-duct diseases. Thousands of children already owe their emancipation from such diseases to the regular ocular examinations made in schools. One need not hesitate to say that every board of health and board of education in this country are committing a moral and social crime if they do not insist upon annual, systematic examination of school-children's eyes, ears, noses and throats.

In many cities a conflict has arisen between the board of education and the board of health as to which one shall undertake this work. The board of health may claim that they have no money to hire a sufficient staff of doctors, or even nurses, to perform the work, while the board of education may claim an insufficiency of funds, or an unwillingness to place this additional work on the teachers. And thus between these two stools the children come to the ground.

In order to make the *examination of school children's eyes by school teachers* easy and practical, Frank Allport has prepared "a visual chart for schools." This chart contains the usual test letters for testing vision. Each line also contains at least one letter for illiterates, which enables small children who do not know their letters to be accurately tested as to their visual capacity.

The lower portion of the chart contains the teacher's instructions.

If an ocular defect be found or suspected the teacher sends a warning form to the parent, thus placing the responsibility where it properly belongs.

If parents neglect the warning thus conveyed, the teacher should, from time to time, endeavor to convince such parents of the advisability of medical counsel. Teachers are urged to impress on pupils and parents the necessity for consulting reputable physicians.

These tests should be made annually at the beginning of the fall term, and should include all children above the first grade.

Each teacher should examine all the children in her own room, and should report the results of such examinations to the principal, these reports to be signed by the examining teacher. The teacher should have two or three assistants, in order to expedite the work, and these can usually be found among the children themselves. One assistant should stand near the test letters and point them out, another should make out the "Warning Cards to Parents," etc.

No teacher should complain of this work, for she is the one who is the most benefited by it. One child who through some uncorrected eye, ear, nose or throat defect continually lags behind his class and becomes idle, mischievous and disturbing will cause the teacher more trouble in the course of a year than would the making of these tests. They are really labor and nerve-saving devices and teachers ought to recognize this fact and encourage them. This has been the case where the tests have been systematically carried out.

The annual, systematic, preliminary examination of school-children's eyes, ears, noses and throats by school-teachers, is an agency of enormous and incalculable benefit to the children, to the parents, to the community at large. Then why not universally benefit by it, especially as the cost is insignificant? The only expenses are the testing charts, which can be purchased for $5 a hundred, "Warning Cards," and the simple record blanks which cost almost nothing. If medical inspectors had to be hired to do this work the lack of funds might prove an embarrassment. But medical inspectors are not necessary, as the teachers can do it perfectly well, and by answering the nine simple questions at least 95 per cent. of serious eye, ear, nose and throat diseases will be detected. This is all the teacher has to do; she is not expected to ascertain the nature of the child's complaint; the doctor consulted will perform that function.

In some communities, especially in New England, they have been trying the experiment of employing one or two school-nurses of exceptional ability and tact, to act not only as medical inspector, but also as school-nurses. They look for defective and diseased children, urge the parents to take them to their doctor and then do what they can to follow out the doctor's instructions. They also assume supervision over hygienic and sanitary conditions in the schools and in the homes of the children. In many places the eye, ear, nose and throat tests are made by these school-nurses and the plan has worked admirably. Indeed, the entire plan of substituting trained, experienced and tactful school-nurses for medical inspection in small places has much to recommend it, and is well worthy of a trial.

Albinism of the Eye.—This subject is of some importance to the student of infantile anomalies. As W. F. Hardy* remarks, the eye is probably the richest pigmented organ of the body, hence when pigment is lacking as a whole the eye is conspicuous, owing to its loss of coloring matter. Not only the eye, but the whole facial aspect is characteristic and gives to the afflicted individual a most peculiar appearance. Albinism in the eye is but a part of a general lack of pigment in the whole of the body. Geoffrey St. Hilaire divided albinism into complete, incomplete and partial. Such a classification may, with propriety, be applied to the eye. The first two classes include varying grades of pigment deficiency, while in the last there is a considerable reduction or total absence of pigment in a part of an organ, the rest being normal. Partial albinism is at times noted in the eye. Dark races seem more disposed to the affection than lighter races. The first published accounts of the trouble were in the beginning of the eighteenth century. Wafer in 1704 found the first albinos in Panama. Blumenbach in 1784 directed notice to the presence of albinism in Chamonix and was the first to draw attention to the fact that the reddish color of the pupil is due to this cause. Early travelers in Africa noted cases in Guinea, Algiers, Madagascar and the Congo. Quite a number were found on the African west coast, a few in Central Africa, and none on the east coast. De Paul in 1774 thought that albinism was found only in the regions 10 degrees north and south of the equator and that it did not occur in Europe. Other beliefs that had wide acceptance for a time were that negroes mainly were affected and that female albinos were prolific, while the males were sterile.

It is well known that all the uveal pigment is not laid down at birth, that the irides are bluish, and during the first year become darker, the increased pigmentation taking place in the stroma. The

*Am. Encyl. of Ophthalm., iv, p. 2951.

choroid at birth, according to Kölliker, is also devoid of pigment. Albinism has been noted as a family affection. Butler reported a family where three out of four children were albinos. The father and mother were normal but first cousins. Heredity is a prominent factor, though LaGleyze thinks that consanguinity is the most important factor in a majority of the cases. The transmission of albinism is not constant; it may skip one or more generations. In some families all the children are albinos, while in others some of them will be albinos and the rest normal. Blumenbach, Darwin and others found that albino animals are usually deaf. Absence of the organ of Corti and atrophy of the auditory centers were found in an albino dog by Pawitz. Whether there is any connection between the ocular and aural conditions is an open question. The attitude of the albino is striking; there is photophobia, the head is bent forward, the brow corrugated, the lids half-closed and the hand is often held to shield the eyes in a bright light. The conjunctiva is congested and the iris red, the radial striations being plainly seen. The color of the iris depends on the amount of light, red predominating when this is intense, and violet-gray in a dim light. There is nystagmus and frequently strabismus. The association of these is so frequent that a trinity of albinism, nystagmus and amblyopia is referred to (Seefelder). Nystagmus is usually horizontal with large oscillations, the rapidity being between 60 and 100 a minute. The movements may be rotary or mixed. Two explanations are given for the nystagmus, one that it is Nature's protection, saving the macular pigment from being "burnt up" by the intense light. The other is that it is due to amblyopia. The amblyopia, which often cannot be explained by the refractive error, has been shown recently to be due, at least in some cases, to an absence of the fovea. Fritsch found the fovea absent in an African albino. The pupil is small and dilates very little in diminished light. The reflexes are present but feeble. Corectopia is occasionally observed. With the ophthalmoscope the disc is reddish, at times deeper in color than the fundus; at other times it is gray. Usually the disc can only be located by the confluence of the retinal vessels (Mayerhausen). The choroidal vessels are made out beneath the retinal and no pigment is between them. In the most pronounced grades of albinism the hair, eyelashes and eyebrows are fine and downy and either perfectly white or possess a pinkish or yellowish tinge. The sclera is thin and offers slight resistance to the penetration of light. The skin of the lids, as of well asother parts, is thin, soft and white. Visual acuity is always reduced, due to several factors, chief among which is lack of fixation and excess of light. The great diffusion of light and the inability of sustained fixation must operate in preventing clear definition. If we accept the possibility of the absence of the fovea, then the amblyopia, the nystagmus and even the strabismus are at once explained. Color vision and the fields of vision are usually normal. Myopia is said to be the commonest refractive error. LaGleyze found no preponderance of myopia over hyperopia in his cases, but did find an astigmatism of about 4 D.

usually present. In the milder grades of albinism the condition may improve as time goes on. Streatfeild quotes the case of a woman, aged 36, who stated that until she was 14 year old she was an albino, but from then on she became pigmented. This, of course, could only occur in incomplete albinism. In the complete forms no such change takes place. Blumenbach was the first to describe the absence of pigment in animals. Wharton Jones noted the absence of pigment in the hexagonal cells of the retina. In human eyes there is always a little pigment in these cells, though it is absent from the stroma. The supposition that the retinal epithelium is absent (Buzzi) has been disproved by anatomical examinations. Absence of pigment in the whole uveal tract and stroma of the choroid was found by Bruecke. In 1905 Nettleship showed sections of the retina containing pigment only at the macular region. Partial albinism has been frequently described where a portion of the iris, choroid or retina was without pigment, the remainder being normal. Cases of absence of pigment in the fundua, while the iris, eyebrows and lashes were normal, are described by Nettleship. Thompson described a patient with ocular albinism, dark hair, eyebrows and lashes and a dark, muddy complexion. The eyes were perfectly albinotic, iris and fundal pigment absent. A myopia of 5 D. and nystagmus were present. Nothing was found in the family history and consanguinity was denied. The condition known as *vitiligo of the iris*, described by Müller as a form of partial albinism, is hardly correct. Numerous small, round or elongated white dots are scattered over the iris, corresponding with excavations in the stroma.

DISEASES AND ABNORMALITIES OF THE EYELIDS

The infantile lids contain a larger percentage of fat and loose areolar tissue than is supplied to the adult. They are consequently prone to excessive swelling in the presence of inflammatory changes, as seen in *ophthalmia neonatorum*, after injuries, etc. Apart from considerations such as these there are few infections of the infantile eyelids that are not found in later life. For example: most forms of *blepharitis* are common to both youth and age and their pathology and treatment are much the same.

Coloboma of the eyelid rarely occurs in the patient as the only ocular defect. These fetal clefts are generally associated with dermoid tumors, iris coloboma and other structural anomalies.

Epicanthus.—This is, as W. F. Hardy* shows, an abnormal development of a fold of skin at the inner angle of the eye due to the excessive development of the skin over the root of the nose. The fold passes from above downwards from one orbital margin to the other. Its edge is concave with the concavity directed outwards. The concave edge is free. The fold is of varying width in individual cases and not always equal in the two eyes. It hides the caruncle and even a goodly portion of the lids. The fold may be obliterated by pinching up the skin over the bridge of the nose. The condition may give to the child an appearance of apparent strabismus. At times an actual strabismus is present. The lachrymal puncta are often hidden by the fold. A probe may be passed beneath it showing that there is no connection between it and the lid margins or caruncle. The folds represent simply duplicatures of skin which are in direct connection with the skin of the bridge of the nose. Epicanthus is a rather common anomaly. It is usually bilateral, von Ammon alone describing a unilateral occurrence.

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* Am. Encyclopedia of Ophthalm., iv, p. 2791.

In mild cases with the development of the bridge of the nose the condition tends to correct itself.

Typical epicanthus is always found at the inner angle. Because of the similarity of a condition which was observed at the outer angle. Sichel and Chevillon described it as *epicanthus externus.* The absence of similar observations makes it improbable that a true external epicanthus occurs as a separate entity. The presence of a fold at the internal canthus gives the child a somewhat sleepy appearance, due probably to the fact that the palpebral aperture is narrower than usual. There is often noticed a subnormal movement of the eyelid due to a partial ptosis or weakness of the levator. A condition somewhat analogous to epicanthus is normal to the Mongolian race in which the bridge of the nose remains flat. Those children with epicanthus have therefore been referred to as *Mongolian types* and have been thought to represent examples of atavism. An admixture of Mongolian blood has also been suspected. Both of these suppositions can in most cases be positively ruled out. The spontaneous cure due to the growth of the nasal bridge certainly speaks against such views. The influence of heredity is quite marked.

One of the commonest of facial characteristics handed down from a normal parent to his offspring is the configuration of the nose. Therefore it is not especially remarkable that epicanthus should occur commonly in many members of a family. It is only the less marked grades of epicanthus which undergo spontaneous cure, the more marked cases are frequently associated with other congenital defects, prominent among which is ptosis. The connection of these two defects often manifests a marked hereditary tendency. Huettemann published his observations on congenital ptosis with epicanthus in three generations of one family. Two brothers affected were illegitimate sons of a father likewise affected. One brother had four living children of whom three were affected. The other brother also had four children, three of whom were affected. Except in one case no disturbance of the other ocular mucles was present. Examination of the electrical reactions in three cases suggested the absence or imperfect development of the levator. The unaffected children resembled the mothers. Steinheim reported a similar series of cases showing the relationship of epicanthus, ptosis and heredity. Sichel-Vignes saw ptosis and epicanthus in 13 persons belonging to four generations.

When these cases do not undergo spontaneous cure, as certain of them do, an (rather simple) operation is called for.

Congenital ankyloblepharon is a union of the margins of the lids throughout part or all of their extent. In the former case it is designated as *blepharophymosis* and in the latter as true ankyloblepharon. It is commonly found accompanying anophthalmia and microphthalmia. Where the union is due simply to a failure in the normal separation of the lids in the latter part of intra-uterine life, such adhesion is purely epithelial. Where the lids are firmly adherent it is usualy the result of a pre-existing ulcerative condition. Some cases are attributed to injury in pre-natal life. This is given as a cause, especially in those cases characterized by the union of the lids by a filament. Fingernail injury may be a causative factor. In blepharophymosis there is a diminution in the breadth of the palpebral fissure as a rule at the expense of the outer angle. It is worthy of note that in the latter condition enophthalmus and anophthalmus are frequently present.

It only remains to mention without further detail the quite rare congenital *symblepharon* (adhesion of lid to the eyeball); *entropion*, eversion and *ectropion*, inversion of the eyelid.

Epitarsus, an apron-like fold of conjunctiva on the under surface of the eyelid; *trichiasis*, irregular arrangement of the lashes; *distichiasis*, supernumerary rows of cilia, and *accessory eyebrows* are also occasionally seen as congenital abnormalities.

Tumors of the Eyelids in Childhood.—Although most of the neoplasms—benign and malignant—that are seen in adult life also affect the lids of children there are several that are of especial interest. Of these one only will be discussed here, *viz.*, angioma.

Angioma. Mother's Mark.—Several forms of vascular tumor are seen in the infantile lid. The simple *vascular nevus* or "mother's mark," is a congenital condition resulting from excessive development of capillaries, and appears as a bright-red spot, varying in size from that of a pin-head to the entire area of the surface of the lid. It occasionally disappears spontaneously, but is usually permanent. It rarely increases in size.

Telangiectasis consists of a collection of enlarged capillaries, arterioles and venules in the skin and subcutaneous tissue, which may exist at birth but generally appears later, and in either case tends to increase.

Cavernous angioma forms a distinct tumor consisting of cells and sinuses and enlarged vessels, with a framework of connective tissue. It may be congenital but more frequently originates after birth, and is sometimes developed from the preceding variety. These tumors can generally be emptied by pressure, but occasionally pulsate, if chiefly arterial in character.

Treatment consists in obliteration of the vessels, destruction by cauterization, or removal with the knife. Small superficial nevi may be successfully treated by caustics. In the case of infants, vaccination at several points will often excite sufficient inflammation to obliterate the vessels. A larger growth may be treated by inserting a fine thermocautery needle obliquely under the skin at numerous points around the base. Coagulating injections are not without danger, and ligatures are likely to cause suppuration and leave cicatrices. Cavernous angiomata are frequently encapsulated, when they can be safely enucleated. In other cases removal should be accomplished by incision carried well into the sound skin. A blepharoplastic operation may be necessary. Carbonic acid snow has been successfully employed in a number of cases. Capauner* has used carbonic acid snow very successfully in two cases of large angiomata of the lids in little children. Applications were made at intervals of about 10 days to allow all inflammatory symptoms to pass away between treatments. The snow is forced into a small glass tube 1 cm. broad by 1 cm. long and about 1 mm. thick, by means of a wooden plug. Pressure upon the plug forces out the snow as desired without danger of injury to the conjunctiva. Toleration is established in the skin after a few applications, so that the time of treatment may be lengthened from 30 to 60 seconds. Knapp† reported the case of an 11 months old infant with an angioma of the eyelid characterized by thickening of the skin and a mass of large blood-vessels. The growth involved the edge of the lid, making excision with the knife undesirable. One application of the carbonic acid snow caused the growth to shrivel up and drop off. Risley‡ reported the case of an angioma of unusual dimensions, and the method employed in its removal, which is of interest. The patient was an 11 weeks old infant, and the tumor occupied about three-fourths of the entire length of the right lower lid. The tumor was soft and fluctuating, but grew tense when the child cried, so that bursting of the much-thinned pellicle of enveloping skin seemed imminent. The method of procedure adopted for its removal is thus described by Risely: "A single electrolytic needle was inserted at many points into the base of the tumor, at first superficially, and gradually made to penetrate its mass more deeply, but only in its deeper portion, in order to secure a firm coagulum, first in the region of the emerging vessels at its periphery, and then over the entire base. Under the electrolysis the entire mass became hard, lost its fluctuating quality and shrank. The surface was then covered with a thick coat of collodion. In 48 hours the rounded, overhanging borders had disappeared, the surface was corrugated and much flattened. In a week the electrolysis was repeated, and later with multiple needles three times at intervals of a week or 10 days, but without any marked improvement beyond that secured by the first attempt. The tumor remained hard and quite dense at the center, but showed an unmistakable tendency to spread laterally, and it became obvious that some more radical procedure was required if a cure was to be effected. Deep electrolysis was again repeated and the following day an Ericson's suture was introduced.

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* Klin. Monatsbl. f. Augenheilkunde, xlix (November, 1911).

† Arch. of Ophthal. (January, 1911).

‡ Ophthalmic Record (March, 1906).

A large curved needle with an ample eye was threaded with one black and one white heavy silk thread a yard long. Beginning at the nasal extremity of the tumor, the suture was carried vertically upward through it, being careful to include the mass down to the surface of the lid cartilage, but not including it. Then reversing the procedure, the thread was carried through the mass downward to a point 5 mm. from the first, and so back and forth until the entire tumor was enclosed in a series of loops, above and below. The extremity of the loops of white thread were then cut above, leaving them intact below. They were then drawn tightly home and tied. The black loops were then cut below and in a like manner brought firmly home and tied, in this manner effecting a complete strangulation of the entire mass, which sloughed off in about a week without hemorrhage, leaving a granulation mass at each extremity. These were also removed by strangulation with a silk thread, after which the surface cicatrized rapidly, manifesting but little tendency to ectropion."

Infantile Gangrene of the Eyelids. Spontaneous Gangrene. Phagedenic Ulceration. Malignant Edema.—Noma.—This rare condition has been observed by several writers. The disease appears in emaciated infants and children, and is characterized by swelling of the lid, the formation of a pimple which is soon converted into a pustule and is followed by ulceration, and the presence of a thin conjunctival discharge. The skin, conjunctiva, and intervening structures soon break down, and may be partly or entirely destroyed. The ulcer presents sharply defined, undermined edges, bordered by a zone of darkly congested skin. There is greenish pus and a dirty slough. The cornea is opaque and ulcerated and perforation results. The ulceration may spread into the eyebrow and on the cheek. The bacterial cause of the disease has not been determined. The *prognosis* will depend on the time when the patient is brought for treatment and on the general condition. The *treatment* consists in cleansing and antiseptic applications, and supportive measures internally. The administration of diphtheria antitoxin has been recommended. A case following an attack of diphtheria was reported by Marlow* in which there was complete destruction of both the upper and lower lid, including skin, conjunctiva, and all the intervening structures.

Cases of gangrene of the eyelids as a *sequel of measles*, have been recorded by Fieuzal† and others. Stoewer‡ also reports a case of this kind with consequent hemorrhagic diathesis. The case cited is that of a three year old child in whom a small ulcer developed on the right lower lid margin. The child had just recovered from measles. A few days after, the ulcer was noticed, and the lower lid became much swollen and the skin over it dark-blue in color. At the same time there was a constant trickling of blood from the lid aperture. Examination under chloroform showed that the bleeding came from the general conjunctival surface, no eroded spot being found. Compression failed to stop the bleeding and Stoewer contented himself with a mild application of nitrate of silver to the conjunctiva and the use of a wet dressing. Within the next few days the submaxillary glands became much swollen and hemorrhages were observed on the mucosa of the tongue and in the skin. Eventually the child made a good recovery, and though a triangular area sloughed from the edge of the lid, little deformity remained. Stoewer looks upon the whole process as a local and general sepsis due to the staphylococcus aureus which was found in the lid ulcer. There was no suspicion of hemophilia, and Stoewer considers the hemorrhagic tendency to have been an effect of the septic process. The disease ran the course of typical purpura hemorrhagica.

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* Ophth. Rec. (December, 1901).

† Centralblatt f. prakt. Augenheilk. (1887).

‡ Klin. Monatsbl. f. Augenheilk. (July, 1908); review in Oph. Review (October, 1908).

In Bergmeister's case* gangrene affecting particularly the lower lid occurred with ophthalmia neonatorum. Gonoccoci and streptococci were present. The reporter ascribes the affection to the circulatory disturbance caused by the great tension and swelling of the lids for a week before advice was sought. Tertsch reports a case of gangrene of all four lids in a newborn syphilitic infant. Francke observed gangrene of the upper and lower lids of both eyes in an infant followed by good recovery. No cause could be found other than a cold and damp dwelling house; he accordingly denominated the affection "noma."

Blepharospasm.—Although only a symptom and already mentioned elsewhere yet *spasm of the orbicular muscles in children* is often a serious and troublesome complaint, about which the pediatrist should be well informed. It is present in practically all cases of *phlyctenular conjunctivitis and keratitis* and often persists long after the subsidence of the acute conjunctival or corneal symptoms. In such cases careful examination will often show a minute fissure at the outer (occasionally at the inner) canthus. The patient with reflex blepharospasm shuts the eyelids tightly, strenuously resists efforts to open them, hides the head in a handkerchief or pillow, and dreads exposure to light.

Its *treatment* naturally varies with the cause of the complaint. In children effective, but harsh treatment of persistent spasm is in holding the head beneath an irrigator or cold water tap, or allowing ice water to flow with slight force over the closed eyelids. In addition stretching the lids with elevators or other instruments is effective.

R. D. Gibson instills a single drop of 4 per cent. solution of cocain into the eye, to prevent undue irritation of the parts, and follows this with the introduction of an eye speculum to expose the eye to the light and air for a period varying from 3 to 10 minutes once per day. The setscrew of the speculum may be advanced a little at a time until the full tension of the spring is exerted in stretching the lids wide open.

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* "Ophthalmic Year Book" (1909), p. 283.

INFANTILE AND JUVENILE DISEASES OF THE CONJUNCTIVA

The *conjunctiva*, a most important mucous membrane, joins, as its name implies, as well as covers most of the parts in the front of the eye. It is a loose, lymphoid structure, continuous with the epidermis at the margin of the lid, and lining the inner surface of the lid, in which location it is known as the *palpebral conjunctiva.* Upon leaving the lids it forms the superior and inferior palpebral folds, and is then reflected onto the eye-ball, where it bears the name of *ocular conjunctiva.* This place of reflection is known as the *fornix conjunctivæ*, or *sulcus*, in which one finds the folds of transmission or *retrotarsal folds.* Upon the abundance and looseness of the membrane in this position, depends the free movement of the eye-ball. When the eyelids are closed the free margins of this membrane come together and form the *conjunctival sac.*

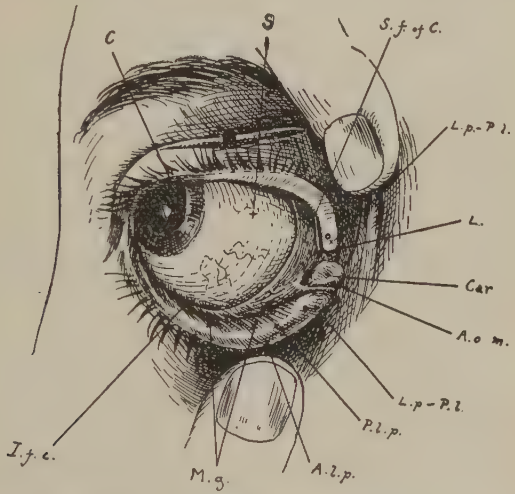

FIG. 99.—The right eye. *C*, Cornea; *s*, sclera with tunica conjunctivæ bulbi; *s. f.* of *c.*, semi-lunar fold of conjunctiva; *L. p.-P. l.*, lachrymal papilla with punctum lacrimale; *L*, lacus lacrimalis; *Car.*, caruncula lacrimalis; *A. o. m.*, angulus oculi medialis; *P. l. p.*, posterior limbus palpebralis; *A. l. p.*, anterior limbus palpebralis; *M. g.*, meibomian glands; *I. f. c.*, Inferior fornix of conjunctiva. (American Encyclopedia of Ophthalmology, Vol. I.)

The structure of the conjunctival mucosa differs but little from that of the adult conjunctiva, but several pathological states require particular mention since they are almost entirely confined to infancy or childhood.

By far the most important affection of this covering of the eyeball is the so-called **ophthalmia neonatorum,** if for no other reason than that it is responsible for from 20 to 30 per cent. of the (unilateral and bilateral) blindness in all countries. About one-fourth of the pupils and inmates of our blind schools, hospitals and asylumns are there because of this infection of early infancy.

This acute inflammation of the conjunctiva, which is usually due to gonococcic infection, begins to show itself on the second or third day after birth. The symptoms are about the same as in gonorrheal conjunctivitis in the adult, except that the process is less severe and the corneal complications less frequent. There is first a redness of the eyelids and a mucopurulent discharge. Slight conjunctival hyperemia is soon succeeded by great swelling of the lids, chemosis and profuse purulent discharge. One eye is generally infected first, and if promptly and thoroughly treated the process is much less severe in the second eye. There is great swelling of the retrotarsal folds, so that sometimes the upper lid becomes spontaneously everted when the child cries, and the fornix appears as a red, suppurating mass resembling granulations.

Inoculation by the gonococcus occurs either during the passing of the child through the maternal passages, or shortly after and, in a few cases at least, *in utero*, since the disease was present at birth. When labor has been slow, and especially in face presentations, infection is much more common.

The *diagnosis* of ophthalmia neonatorum should present no difficulty. *Any redness or discharge about the eyes of an infant occurring during the first four days after birth* is to be regarded as of gonococcic origin unless a bacteriologic examination shows it to be otherwise.

While it is always a serious disease, if recognized in the very beginning and properly treated, few eyes will be lost, although a small nebula often remains on the cornea. On the other hand if the case is not seen early, or if improperly treated, fully 80 per cent. of the eyes affected will end in blindness, due to sloughing of the cornea.

Credé-Hoerder* thinks that a microscopic examination in many cases would show that the diagnosis of gonorrheic ophthalmo-blennorrhea is made too frequently. The non-gonorrheic form presents the following aspect: Late appearance of symptoms, agglutination of the lids, redness of the lid borders and their surroundings, moderate edematous swelling of the upper lid, purulent or sero-purulent secretion, redness of the conjunctiva, thin deposits on the palperbral conjunctiva, cornea clear. Its course differs very much from the gonorheic form by the intactness of the cornea and the scanty, more serous secretion. Microscopically the author found Fraenkel's pneumococci and B. coli. The *treatment* in his cases consisted in irrigation with boric acid solution and; in a severe case of pneumococcic blennorrhea, which commenced on the eighth day after birth, in instillations of acetate of silver 1.3 per cent. on the first and fifth days of the disease. He considers the careful treatment of the otherwise harmless non-gonorheic ophthalmo-blennorrhea of great importance in preventing later chronic conjunctivitis, which may be very difficult to cure.

Quite early after Neisser's discovery of the gonococcus it was recognized that in many cases of ophthalmia neonatorum this organism was not to be found. And it was observed that these cases, though often beginning acutely, commonly took a comparatively mild course, with little danger to the cornea. The incubation period of these cases was found to be somewhat longer than that of the gonococcal cases. In a varying proportion of them organisms such as the pneumococcus, staphylococcus aureus, etc., were found and held to be causative. Still a considerable proportion of the attacks were left unexplained.

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*Deutsch. med. Wochenschr. (Jan. 9, 1913), p. 74.

Treatment of Ophthalmia Neonatorum.—While every pediatrist should be well informed as to the usual routine therapy of this serious infection yet there is no disease in which the services of the experienced ophthalmologist are more acutely needed or at least none in which the responsibility for the proper conduct of the case may be more satisfactorily shared.

In the earliest stages of the disease cold applications are useful. Without interfering more than is absolutely necessary with the sleep of the child, pieces of gauze or linen two inches square and several layers in thickness placed on a cake of ice should be applied at two minute intervals; the piece removed should be destroyed. This process should be kept up both night and day during the early stages of edema if the case is a severe one. The general condition of the patient should be watched, the bowels kept open and the pulse kept down. If pain is severe one of the preparations of opium should be used. Where the lids are greatly swollen a canthotomy may be done, under general anesthesia. With a pair of strong scissors the tissues at the external canthus are cut down to the bone. The hard chemotic conjunctiva can then be seen and scarified in a radiating direction from the cornea. Engorgement of the blood-vessels and pressure on the eye is thus removed. The conjunctival sac may also be irrigated with warm boric acid solution (1 per cent.) or bichlorid solution (1 to 4000).

In the next stage, when profuse purulent discharge sets in, the important thing is to keep the conjunctiva as clean as possible. The cold applications may now be discontinued; the chief aim of the surgeon being to keep the conjunctival sac free from pus. There should be both a day and a night nurse, as it is of the greatest importance that the eye be cleansed as frequently as possible while the purulent discharge is excessive. The cleansing may be done by various methods: Mopping up the pus with absorbent cotton and washing the cul-de-sac with boric acid solution by means of a pipette, perforated elevators, the undine or by keeping the surfaces clean by a continuous stream from a fountain syringe, as advocated by some.

Prophylactic measures show more brilliant results here than in any other disease, and may now be mentioned. The use of vaginal antiseptics before birth lessens the danger of infection. Immediately after delivery the child's eyes should be washed with bichlorid solution (1 to 8000), followed by the instillation upon the cornea of one drop of a 2 per cent. solution of silver nitrate. This procedure, known as Credé's method, has proved to be of such distinct value in preventing gonococcal infection that in many countries its practice is made obligatory by law.

Geo. H. Thompson* agrees with those observers who believe that the mildness of gonococcal ophthalmia in the infant is explained by supposing that the mother confers a strong degree of immunity upon the child. He does not believe that the milder disease in the infant is due to the fact that the infection has long lain dormant until roused into activity, whereas in the adult it occurs at the height of an attack of acute urethritis, when the infective powers of the microörganism are presumably greatest. The author regards cases which occur before the second day after birth as due to intra-uterine infection, and those after the tenth day, to secondary infection. He thinks that the corneal ulceration is usually caused by traumatism from the fingers, either of the infant or of the attendant. Hence (quite consistently), he advises, that in the treatment of the malady the baby's arms should be confined, so that he cannot reach his eyes, and in applying lotions, that the use of undines or of syringes be avoided. There is another reason for not employing syringes (not mentioned by the author), namely, the danger of infecting one's own eyes, of which unfortunate casualty the reviewer has witnessed a number of instances.

As regards treatment, silver nitrate is not used by Thompson, who depends upon 25 per cent. argyrol or 4 per cent. protargol. Despite the fact that some (including the writer) think lightly of its germicidal properties, Thompson has always been satisfied with argyrol in suppurative conditions about the eye. The eyes should be kept clean with boric lotion or normal saline. The slighter corneal complications are treated with hot fomentations, the local application of carbolic acid or of tincture of iodin, the operation of corneal section being reserved for the more serious cases. He does not believe in the application of either atropin or physostigmin.

He mentions a surprising fact reported by Derby, *viz.*, that in a series of cases reported from the Massachusetts Charitable Eye and Ear Infirmary 23 per cent. were unilateral. This is very different from the experience in Europe, where most cases eventually become bilateral. Indeed, one English observer went so far as to assert that unilateral cases are never seen.

Comparing the results of cases treated in private and in hospital, according to Cheney, Thompson makes some interesting remarks. Among 116 babies treated in the year 1909 at the Massachusetts Charitable Eye and Ear Infirmary only six became blind, and all of these were brought after ulceration was well established. On the other hand, in eight American cities, of 61 medical men, each of whom was confronted at least once during 1909 by a case of ophthalmia neonatorum, 39, or over 64 per cent., neither asked at any time for expert help, nor transferred the cases to hospital, but "invariably tried their inexpert hands at restraining the disease which they had failed to prevent." These physicians treated 44 cases, and they failed to save the sight of nine babies. "For these physicians the best that can be said is, that they reaped the result of their own laxity in 20 per cent. of their eye cases; or, in other words, they failed to prevent blindness in every fifth case."

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* Abstract in Br. Jour. of Ophthalm., from the Boston Med. and Surg. Jour. (May 25, 1916).

As showing the unwisdom of giving a definite prognosis, Thompson mentions a couple of cases, in one of which a corneal ulcer developed when discharge had practically ceased, and in the other where the baby, under similar circumstances as regards discharge, developed fatal meningitis.

Before discharging a case Thompson takes two negative smears at intervals of 48 hours. He mentions the circumstance that gonococci have been found in the conjunctiva 25 days after the eyes were apparently well, and 60 days after the onset of the discharge.

Thompson whole-heartedly advocates the use of silver nitrate, 1 per cent., as a prophlactic, although he mistakenly states that these drops were originally recommended by Credé. In point of fact, as well known, the Leipzig professor employed and advocated 2 per cent. silver nitrate.

The legislation in the various states regulating the report and conduct of cases of ophthalmia neonatorum has been studied, collected and collated by Dr. Frank Allport of Chicago, Chairman of a Committee of the American Medical Association. Pamphlets embodying these exhaustive investigations may be had from the office of the Journal in Chicago.

Phlyctenular Conjunctivitis.—Also known as *phlyctenular ophthalmia. Scrofulous or strumous ophthalmia. Eczematous conjunctivitis. Lymphatic ophthalmia or conjunctivitis.* This is one of quite a distinct class of conjunctivitides which are to be regarded as expressions of dyscrasiæ depending both upon the introduction of pathological germs from without as the causative factor, and upon the condition of the general system and the state of the nutrition as their most important factors.

The dyscrasia formerly called "scrofula" or "struma," but which we now know to be mostly tuberculous, manifests itself in the conjunctiva more frequently than any other disease of malnutrition, and is especially frequent in children, though adults are by no means free from it. The appearance of vesicles on the conjunctiva is not, of course, a certain indication of established "scrofula," as they often occur during a temporary lowering of the nutritive powers in children who are apparently strong and show no evidence of the dyscrasia elsewhere, and there are cases of pronounced and severe forms of strumous disease in which the conjunctiva is slightly or not at all affected. Still, the appearance of these vesicles on the conjunctiva can be accepted as a certain sign of faulty assimilation, and generally of an impoverished condition of the blood.

It would seem probable too, that in some instances at least, the vesicles are manifestations of a derangement at the nerve-centers analogous to, if not identical with, that causing herpes zoster. We can hardly account otherwise for the very pronounced nervous symptoms, the severe pain, lachrymation and photophobia, which we not uncommonly notice. There is no other disease which varies so widely in the intensity of its symptoms; and what is still more remarkable, the subjective symptoms do not seem to bear any direct relation to the objective manifestations. Frequently a minute vesicle, especially if situated on the ocular conjunctiva near the corneo-scleral margin, will be associated with the most intense pain, photophobia, and lachrymation, persisting for days and weeks, while two or three large ones scattered over the conjunctiva elsewhere give rise to comparatively little inconvenience. This is due both to the extreme susceptibility of the nervous system, and the pressure made directly on the filament of a nerve by the exudation. This latter is more apt to be the case where the vesicle is situated on the conjunctival layer of the cornea, where the nervous supply of the fifth pair is more generous and the arrangement of the terminal filaments among the epithelial layers is such as to lead more readily to such pressure. In the same way we may account for differences in the severity of various attacks in the same person, one being mild, and another, with the same objective appearances, very severe.

The epithelium at the apex of the vesicle soon separates, the underlying tissues becomes softened and breaks down, and thus a minute gray ulcer is produced. New epithelium soon forms over the ulcer, however, and after healing no scar remains. The characteristic pathological change is what appears to be a vesicle varying in size, from that of a pinhead or less, to a bleb 3 or 4 mm. diameter and approaching that of a bulla. The associated conjunctival vascularization may be only a bunch of fine vessels running from the equator of the ball forward to unite at the base of the phlyctenula, the remainder of the conjunctiva being perfectly clear, or it may be general and diffuse, approaching that of a mucopurulent conjunctivitis. Though usually single, there may be any number of these phlyctenulæ, and sometimes they form a circlet around the base of the cornea. There is frequently associated with the conjunctival disease a swollen condition of the edges of the lids, and sometimes of the whole lid. The discharge may be either watery or mucopurulent. The discharge is very acrid in some cases and causes an eczema of the cheeks, lips, and the inside of the nose. In badly nourished and ill-cared-for children the whole face is sometimes covered with scabs and excoriations as a result of this irritation. When there is persistent blepharospasm as a result of the intense photophobia there will frequently be seen excoriation and ulceration in the folds of the skin at the outer canthus. There may be even a total eversion of the lids (*ectopia conjunctivæ*) when the blepharospasm is very intense and obstinate. Actual pain, aside from the photophobia is not usually great, but the photophobia is usually extreme in children; the patient hides in a dark corner or buries his head in a pillow, making an examination very difficult. The child often presents a characteristic "strumous appearance," being pale and thin, or flabby. Enlarged cervical lymphatic glands, adenoid vegetations in the pharynx, thick lips, eczema of the nose and upper lid, and purulent otitis media are often seen in these children. Although the disease has long been regarded as of strumous origin, it has always been difficult to trace tubercular association.

There is apart from this picture also a difinite lesion, *tubercle of the conjunctiva*, infrequent certainly in comparison with phlyctenular conjunctivitis, but well characterized, and easily differentiated from it, showing the presence of the tubercle bacillus. Phlyctenules on the other hand do not present tubercle bacilli; at least their presence has been rarely demonstrated. In cases of phlyctenular ulcer, the opsonic index is usually very low. This is probably because it is the toxin which has the power of setting up phlyctenules, whereas in tubercle of the conjunctiva, the bacilli are present.

Hanford McKee* says that in many cases of phlyctenular conjunctivitis lacrimation is so severe that the conjunctival sac is almost constantly flushed, consequently the bacteriological examination is often negative. In a series examined at the Montreal General Hospital, the following results were obtained: Morax-Axenfeld diplobacillus, 27 times; staphylococci, 14 times; bacillus xerosis, 3 times; negative, 23 times. What strikes one here is the comparatively large number of negative results. McKee believes that it is just as sound to attribute cases of conjunctivitis to the bacillus xerosis, because that organism is frequently found in the inflamed conjunctival sac, as it is to attribute phlyctenular conjunctivitis to staphylococci because the latter are found in many of the cases.

In the **treatment of phlyctenular conjunctivitis,** it must be remembered that as the disease is largely the local expression of a systemic condition, it is the surgeon's duty to find the cause and remove it, while at the same time local treatment is employed. Only the most nutritious articles of food should be allowed, such as milk, eggs, beef, mutton, and fowl; no pork or veal, very little bread or potatoes, and no sugar or fat; tea and coffee only in moderation. A child with phlyctenular conjunctivitis should not be kept in-doors nor in a darkened room, even though the photophobia is great. On the contrary he should have plenty of fresh air and sunlight, the eyes being protected with colored glasses. The skin should be kept clean and the bowels open. In regard to drugs, iron in some form has been most generally employed. For a child perhaps the best preparation is the syrup of the iodid of iron, in doses of from 15 to 30 drops, given three times a day, in water. In those cases which do not respond to this general treatment, the salicylate of soda in large doses (3 gr. every four hours, for a child of five years). The effects must be carefully watched, depression and tinnitus being signals for the temporary interruption of the doses. This treatment should be discontinued if improvement does not follow in a few days.

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* Am. Encyclopedia of Ophthalm., ii, p. 832.

For *local treatment* atropin is indicated where there is much irritation; cocain or holocain can be used occasionally. If, as is often the case, the vesicles have burst at the time of the first examination the local use of mercury is indicated. Finely powdered calomel dusted onto the ulcers, or a very little of the ointment of yellow oxide of mercury, 1 gr. to the dram, placed in the conjunctional sac are probably the best preparations. Calomel should not be used if the patient is taking iodid of potassium internally, since the potassium iodid in the tears, uniting with the calomel, forms double iodids that cause irritation. The treatment with the yellow oxide should be continued for a week or more after all signs of the local inflammation have disappeared. Concomitant lesions of the nose, skin, ear, pharynx, and lymphatic glands should receive proper attention, tuberculin if indicated, and finally the patient's refraction should be examined, and any existing ametropia corrected.

Follicular conjunctivitis or simple granular lids is of especial interest to the pediatrist because of its prevalence among *school children.* Essentially it consists of enlargement of the adenoid tissue of the conjunctiva, which takes the form of small, round or oval translucent bodies, that are seldom larger than a rapeseed and resemble follicles. They are more numerous in the lower than in the upper fornix, and they lift up the conjunctiva, forming small elevations, often arranged in rows parallel with the folds of the membrane. They are reddish or yellowish in color, and the conjunctiva beneath them may be thickened but is soft and pliable. They are simply the enlarged or hypertrophied normal papillæ or follicles of the membrane. The disease frequently follows a purulent or mucopurulent conjunctivitis. Among school children examined by Stephenson in 1895, he found this condition present in 75 per cent. Trachoma never develops from simple granular conjunctivitis, and no matter how long the inflammatory process continues, there is no tendency to a destructive process, the conjunctiva being left intact. It has been a matter of considerable dispute whether or not there is any *relationship between folliculosis and trachoma,* but it is the opinion of ophthalmic surgeons that they are clinically distinct diseases although histologically there is no strict demarcation between fresh follicles and fresh trachoma bodies. In differentiating the two diseases, there are clinically certain marked differences. Folliculosis is not contagious, when there is no discharge, while trachoma is usually contagious. Folliculosis is not associated with corneal complications, or with structural changes in the tarsal plate, and it never causes trichiasis, entropion or ectropion. Trachoma, on the other hand, is often associated with pannus, corneal ulceration, trichiasis, entropion, or ectropion. Trachoma may occur at any age,

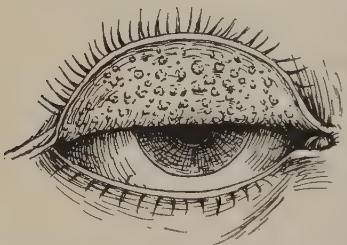

FIG. 100.—Follicular conjunctivitis. (American Encyclopedia of Ophthalmology, Vol. iv.)

while folliculosis is rarely seen after the twentieth year. Stephenson describes the conjunctival appearances in each disease as follows:

False, or Follicular Granulation.	*True, Trachomatous or "Sago-grain" Granulation.*
Oval or roundish transparent bodies, the diameter of which, seldom or never exceeds 1 or 1.5 mm. They often show a faint-yellowish hue, and are usually arranged in rows. Their tendency is usually to remain discrete, that is, separate from one another. They are always larger and better marked in the lower fornix.	Round, opaque, ill-defined bodies, of grayish-white color, and extreme friability. They are firmly and deeply imbedded in the conjunctiva, their diameter frequently reaching 2 mm. or more. Their tendency is to become confluent, thus forming areas of trachomatous material. They are always larger and more numerous in the upper fornix.

It must be borne in mind that in some instances folliculosis may be grafted on true trachoma, making a *mixed* form.

It has been frequently stated that follicular conjunctivitis is caused by unhygienic surroundings, or by vitiated air, but Stephenson has shown that it occurs as frequently among the children of the rich, and in the most favorable surroundings, as it does among the poor. It is often found among the children of farmers, who have no lack of fresh air and sunlight.

The **symptoms** of folliculosis are those of a chronic congestion, or of catarrhal or purulent conjunctivitis, according as the one or the other process in the conjunctiva is more active. There is more or less discomfort about the eyes, and inability to use them, especially by artificial light. The lids feel heavy, and if there is considerable secretion the edges of the lids will be stuck together on waking in the morning, and crusts will form along the roots of the lashes.

The bacterial forms present in this disease are mostly *Morax-Axenfeld*, *Koch-Weeks bacillus* and the *pneumococcus*.

Treatment must be directed towards reduction of the hypertrophied papillæ, and to combat the catarrhal condition if present. When the amount of secretion is but slight, the milder astringents are used: A 0.5 per cent. solution of nitrate of silver; or zinc sulphate, 2 gr. to the ounce, used as a collyrium twice a day is sometimes sufficient. If the discharge is more abundant the stronger irritating astringents will have a more pronounced effect. A smooth crystal of the sulphate of copper rubbed over the exposed surface of the everted conjunctiva causes a temporary hyperemia which tends to improve the nutrition of the parts and to stimulate the absorbents. This application can be repeated as often as every other day, but usually twice or even once a week will be sufficient. An ointment of the subacetate of lead, 1 per cent. applied to the everted conjunctiva once a day, followed by massage is recommended by Stephenson. *Brown ointment* used in conjunction with lid massage is usually very effective. To obtain the best results this ointment should be prepared by making the ordinary dilute citrine ointment with unrefined or brown cod-liver oil instead of with the usual excipient, and this again diluted with from 30 to 40 per cent. of refined cod-liver oil. A small quantity of this salve should be placed in the lower cul-de-sac, and then distributed over the anterior surface of the eye-ball by having the patient rotate the globe in various directions. The upper lid is then gently massaged with the finger from one to three minutes, the patient, meanwhile, turning the eye-ball well downward. The lower lid should be treated in the same manner while the globe is rotated upwards. The surplus ointment (which is of a dark-brown color), should not be washed off the lashes and lid edges for an hour or two after the rubbing because its local, mildly corrective action seems to be of value in these cases.

The general health of the patient should receive attention in all cases, and after the disappearance of the disease the condition of the refraction should be examined and any errors corrected.

Membranous or Diphtheritic Conjunctivitis.—See "Ocular Relation of Diphtheria" in this chapter.

DISEASES OF THE LACRIMAL APPARATUS

By reference to the accompanying illustrations of the anatomy of the child's eye it will be seen that this important group of organs is divided into a secretory and an excretory portion. The former includes not only the lacrimal glands, but the mucous glands of the conjunctiva. As a matter of fact, the moisture that commonly cleanses the ocular and conjunctival surfaces is contributed by the mucous follicles of the conjunctiva, while more copious supplies (tears) are furnished by the lacrimal gland. The latter is of the salivary variety, of a reddish-gray color, and consists of an upper and lower lobe, incompletely separated from each other by the anterior tendinous expansion of the levator palpebræ superioris. The upper lobe is larger, and more compact than the lower; it is oval in shape, and measures about 20 to 25 mm. in length, and 12 to 14 mm. in thickness. The gland is situated in a depression beneath the external angular process of the frontal bone; its upper surface, which is convex, lies close to the periosteum of the orbit, to which it is attached by loose connective tissue; the under surface rests upon the eyeball at the superior fornix toward the external canthus. This gland secretes a slightly alkaline fluid containing much sodic chlorid, which is "sprayed" onto the globe through a fan-shaped array of from 7 to 12 ducts opening at the outer aspect of the superior fornix.

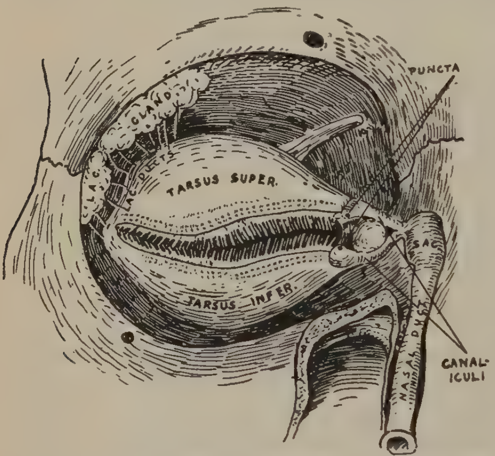

Fig. 101.—Lacrimal apparatus. (American Encyclopedia of Ophthalmology, Vol. i.)

The blood supply of the lacrimal gland is from the lacrimal branch of the ophthalmic artery.

The sensory nerve supply to the lacrimal apparatus is from the lacrimal branch of the ophthalmic or first division of the fifth; the secretory function of the gland is regulated by the sympathetic.

The excretory portion of the lacrimal apparatus consists of the canaliculi, the lacrimal sac, and the nasal duct which is continuous with the sac.

The *canaliculi* have their origin in minute whitish elevations—the *puncta lacrimalia*, situated on the lid-margins about 6 mm. from the angle of the inner canthus, or at the inner termination of the tarsal cartilages. The first millimeter of their course is in a vertical direction—upward in the upper lid, and downward in the lower lid. After this they turn at an acute angle and run 5 or 6 mm. in the direction of the nose. They either meet and form a common canal, or empty separately into the lacrimal sac; generally the former. They are lined by pavement epithelium.

The *lacrimal sac* is 12 mm. long and 6 mm. wide; it opens directly into the nasal duct. Its upper extremity, which has no outlet, lies behind and a little above the *ligamentum palpebræ mediale*, the entire sac completely filling a groove in the lacrimal bone in which it rests. The epithelium of its lining mucous membrane is of the cylindroid variety, and is continuous with that lining the nasal duct.

The *nasal duct* is directly continuous with the lacrimal sac. It is in the child less than 20 mm. long, and 3 to 4 mm. wide, but by no means uniform in its diameter. There is a slight constriction where it joins the sac, and a somewhat expanded orifice where it enters the nose; its narrowest portion being about the middle. Regurgitation from the nasal cavity is prevented by a fold of mucous membrane—the *plica lacrimalis*, or valve of Hasner—situated at the opening of the duct into the inferior meatus just underneath the attachment of the anterior third of the inferior turbinate bone; also by irregular folds of mucous membrane forming imperfect valves along the course of the tube. The epithelium is ciliated. The direction of the nasal duct is downward, outward, and backward; it is enclosed in a canal formed by the lacrimal, superior maxillary, and inferior turbinate bones.

The mucous membrane lining the sac and the nasal duct is attached to the surrounding periosteum by loose areolar tissue which supports a rich venous plexus.

As a *congenital anomaly*, the puncta lacrimalia or the canaliculi may be double, or may be absent altogether.

The tears are drawn into the sac by suction, the motor power being supplied by the tensor tarsi, or Horner's muscle. This is a small, thin muscle about six lines in length, and three lines in width; it lies behind the *ligamentum palpebræ mediale* near the inner canthus. Spiral fibers of this muscle surround the canaliculi; they compress the tubules many times during the act of winking, thus sucking the secretion through the pucta, which are closely applied to the surface of the eyeball. In this way, corneal and conjunctival debris—epithelium, microbes, mucus, tears, dust, etc.—is scraped off the whole globar surface and pushed toward the lacrimal outlet, the cleansing action of Horner's muscle being kept up as long as necessary. Tears and other fluids may to some extent collect in the lacrimal sac before they percolate through the nasal duct into the inferior meatus.

Infantile Dacryocystitis. Dacryocystitis of the Newborn. Congenital Dacryocystitis.—Lacrimal obstruction in the newborn is not as uncommon as it was at one time supposed. Moreover the prognosis is more favorable than similar conditions in the adult. As Jackson, Donald Gunn and others have pointed out, the obstruction is rather one of lack of development than of infection, swelling or stricture of the canal ducts.

The **treatment** should at first be non-surgical and consists in keeping the parts clean, by the use of simple washes like the following: Sodii. borat., gr. xxx; Sol. adrenalin. chlor. (1:1000), fl. ʒii; Aquæ dest., fl. ℥ii.

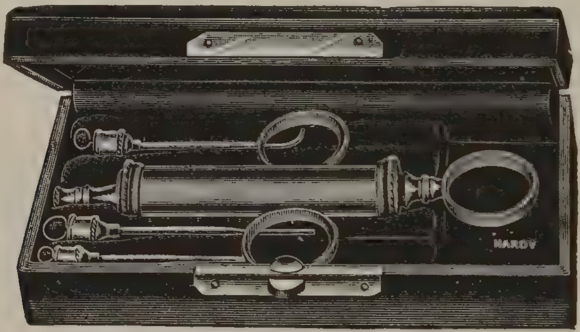

Fig. 102.—Anel's syringe for washing out the lachrymo-nasal passages.

After cleansing the sac, about six times in the 24 hours a few drops of this mixture should be instilled into the eye, to be followed by pressure over the lacrimal sac. Later on, under cocain or a general anesthetic, an attempt should be made to syringe the duct into the nose, first by solution of adrenalin chlorid 1:2000 and subsequently with a 0.02 per cent. of zinc chlorid. Any nasal disorders should be at the same time carefully treated. If this plan be carried out operative measures may, in the majority of cases, be avoided and a cure brought about in a few weeks or months.

In the lacrimal stricture of the newborn J. M. Crawford makes use of pressure applied over the sac and repeats this several times a day as an adjunct to other remedies.

Fage* thinks the *cause of this condition* is arrest of development; or occlusion of the inferior meatus of the nose or the nasal canal. Though the obstruction may originally be of an inflammatory nature, it is probably never due to blennorrhea neonatorum. Three to

*Archiv. d'Ophtalm., xxxi (1911), p. 650.

four weeks after birth a tumor is noticed at the internal angle of the eye, and this may be accompanied by pain and redness. An incision yields mucus or mucopus. It may disappear spontaneously. Treatment consists in expression, probing and incision if necessary.

Fage* has also stated that the infection may originate in the conjunctiva, but it frequently starts in the nasal chambers. He observed an instance in which the disease developed as a complication of inflammation of the ethmoidal sinus, and was cured by incision and drainage. Axenfeld observes that the ethmoidal sinus is undeveloped in the newborn. The appearances may be various; besides the milder forms, which may be mistaken for simple conjunctivitis, cases of medium severity are also met with. In both cure, spontaneous or following simple injection and probing, may take place. Severe cases of long continuance where infection is the principal factor also occur. This may lead to abscess or fistula. Certain anomalies, such as congenital fistula from loosening of the crista lachrymalis, and syphilitic and tubercular periostitis and finally traumatic deformations (e.g., due to obstetric forceps) are to be mentioned.

Cassimatis† reports a case of double purulent *congenital dacryocystitis*. Probing showed extraordinary width of the lacrimo-nasal canal; but led to no improvement. A single injection of physiological serum effected a perfect cure on one side; and two injections brought about a similar result on the other. The results are explicable on the assumption that the injection freed the various openings, especially the one in the inferior meatus.

DISEASES OF THE SCLERA

The *sclera* (*tunica fibrosa*, or *sclerotic coat*) forms about five-sixths (in the newborn, about four-fifths) of the fibrous covering of the eye-ball, and is continuous with the cornea. Indicating the point of blending of the sclera and cornea is a superficial, shallow, circular furrow, the *sulcus scleræ externus*, which is usually filled out by scleral conjunctiva. The fibrous bundles which compose the sclera are generally disposed at right angles to one another, forming a strong, closely woven structure, still further strengthened by elastic and other fibers which run at all angles between the other bundles. Fixed nucleated cells lie between the bundles, particularly in the angles formed by their crossing. The spaces of the sclera resemble those of the cornea, although the scleral organs and components are not so regularly placed.

The thickness of the tunic varies greatly with the individual, being generally thinner in youth and in the female. In the newborn it does not vary so much as in the adult, although it is inclined to be proportionally thicker near the sclero-corneal margin. At the posterior pole it measures 1 mm. or a little more, and gradually decreases toward the equator to about 0.3 mm. The minimum thickness is, therefore, attained immediately underneath the recti muscles, close to the insertion of their tendons; immediately beyond this point, however, the thickness becomes doubled (0.6 mm.) since the muscle tendons at the line of insertion are often as thick as the sclera itself. As a rule, the tendons course obliquely inward into the sclera and disappear farther forward among its fibers. As the sclero-corneal margin is approached the thickness increases until it measures 0.9 mm. At this point, on the inner surface, is located the scleral spur, or annular ligament, composed of circular fibers. It is a wedge-shaped process of scleral tissue which assists in the formation of the sulcus scleræ internus, and serves as the point of attachment of the meridional fibers of the ciliary muscle, and meshwork of the iris angle; it also forms the posterior limit of Schlemm's canal.

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* Ann. of Ophth., xxi (1911), p. 166.

† Clin. Ophtal., xvii (1911), p. 417.

At the posterior pole of the eye, 1 mm. below the horizontal meridian, and about 3 mm. to the inner side of the vertical meridian, is the opening for the optic nerve (*foramen opticum scleræ, porus opticus*, optic entrance, optic canal). Internally the diameter of this opening is about 2 mm.; externally it measures a little over 3 mm. The inner fibers of the sclera are continued across the nerve, between the nerve bundles, forming the lamina cribrosa; the outer fibers are continuous with the dural sheath of the optic nerve.

In addition to the opening for the optic nerve, the sclera is pierced by minute canals, or *emissaria*, through which pass the vessels and nerves supplying the uvea. These canals vary both in size and direction, being in some instances straight, in others quite oblique. Those through which pass the long posterior ciliary arteries, the ciliary nerves, and the vortex veins, course very obliquely; the canals for the latter are about 3 mm. in length. The venæ vorticosæ, usually four in number, are arranged in pairs, upper and lower; they leave the sclera 6 to 8 mm. behind the equator, and their points of emergence are about 90° apart. Loose connective tissue binds the vessels and nerves to the walls of the canals. The oblique direction of these canals prevents bending and tearing of the structures passing through them, during motions of the eye-ball, or in the shifting of the choroid during the act of accommodation.

The scleral layer next the choroid is called the *lamina fusca.* It is a dirty-brown layer, and is probably an extension into the scleral tissue of the choroidal pigment. It shows through the sclera as a bluish discoloration, when that coat is abnormally thin, in some young children, in brunettes, and in most dark races. The sclera itself but rarely contains any pigment, except for the slate-gray spots often seen about the perforations for the anterior ciliary vessels (congenital melanosis of the sclera).

Primary diseases of this external tunic of the eye are relatively rare in childhood. Congenital anomalies (cyst, dermoid tumor, ectasiæ, pigmentation) occur, but they are extremely uncommon.

Blue Scleroties and Brittle Bones.—The syndrome *blue scleræ, fragile bones and deafness* (otosclerosis) is a most curious one. Stephenson* refers to the original observation of von Ammon and to succeeding writers on various aspects of the syndrome. In the year 1841 the former spoke of a peculiar bluish-white coloration of the sclera that may be encountered in cases where the whole development of the eye is backward. A passing reference to a similar condition was made in 1848 by C. A. E. Cornaz, and in 1862 by Sir W. R. Wilde.

Upwards of 40 years later Leslie Buchanan, of Glasgow, described an unusually thin corneo-sclera that he had found on pathological examination of the eye of a girl of nine years, which had been removed on account of an injury. The cornea was three-fifths and the sclera one-third of the normal thickness, and the fibers, although of natural size, were unusually few in number. Bowman's membrane was absent. In 1907 Percival J. Hay, of Sheffield, under the name of "pseudo-coloboma," described a congenital anomaly of the sclera in a stillborn, hydrocephalic child, who presented many other deformities. One eye showed a triangular area, as dark as the pupil, in the sclera on both inner and outer side of the cornea, and in the other eye a similar condition, but on the outer side of the cornea alone. Histological examination showed this unusual appearance to be due to local thinning of the sclera, thereby allowing the dark color of the uvea to be perceived through the attenuated parts.

Stephenson further observes that in 1900 Arthur Eddowes first drew attention to the connection between "blue sclerotics and brittle bones." He had seen a little lad with very dark sclerotics, who, during the two years he remained under observation, had been affected with no fewer than nine independent fractures, not to mention a slight greeenstick fracture of the tibia, which the child's mother treated herself by binding the limb at the seat of the fracture with a necktie. A history of a similar kind was obtained by Eddowes from a girl who possessed remarkably dark sclerotics. She had broken a bone on one occasion by merely falling on the bed. The patient stated that her father's eyes were like hers, and that he also had broken his bones several times, only recently sustaining a fracture of the arm whilst putting his coat on.

Eddowes, then, was the first not only to point to the connection between "blue sclerotics" and fragility of the bones, but also to the hereditary nature of the scleral condition.

The tendency to spontaneous fracture has been widely confirmed since it was mentioned by Eddowes. The assigned cause is often ludicrously insufficient to fracture anything like a healthy bone. One of Burrows' patients broke the femur by sitting down suddenly on the nursery floor, and another fractured the tibia by missing the last step on the stairs. In a girl, aged 12 years, whose case is reported by Conlon, the left hip was broken and dislocated by a fall from a height of 10 or 12 in., and on another occasion her right leg was broken by a fall caused by a dog jumping on her. In Boynton's case the left tibia and fibula were broken by a blow from a child's fist. In the family described by Peters the father had broken his right leg on two occasions, first, when 10 years of age, by falling over a stick, and later by a simple fall, while later still he fractured his left forearm by his head striking his arm as he slipped upon a smooth surface. His second son, when four years of age, broke his left leg by falling from a bench which stood in the porch of the house. Eight years afterwards the same lad broke his forearm by being tripped up and falling flat upon his stomach. At the moment when Peters wrote, another son was in the hospital from a leg fractured from some unknown cause. Speaking of a girl included in the pedigree published in 1910, the mother said, "she had got quite used to picking her up broken" after a slight fall.

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* Ophthalmoscope (1915), p. 278.

In Eddowes' case there were 10 fractures during a period of two years. In a case reported by M. Ostheimer there had been nine fractures between the age of 1½ and 4 years, the child breaking the left femur five times, the right four times, and the left humerus once.

The fragility of the bones applies only to such members of the families as have actually inherited "blue sclerotics," a point upon which H. Burrows has dwelt.

F. A. Conlon has found by means of the *x*-ray that the long bones in his patients had a much enlarged medullary canal and a very clearly defined cortex. All the bones, indeed, showed lack of density and marked atrophy.

In 1908, A. Peters, of Rostock, reported instances of "blue sclerotics" in four generations of one family. The appearance of the eyes was attributed by him to congenital thinning of the sclera. In 1910 Stephenson described the condition in 21 out of 32 members belonging to four generations of one family; and, shortly after, N. Bishop Harman added another generation to the same family, so that a total of over 55 individuals was recorded, of which 31 were the subject of "blue sclerotics." In this extensive pedigree females were mainly affected—82 per cent. as against 44 per cent. of the males.

Behr, who reported a case of conical cornea in association with "blue sclerotics," drew attention to the *dislocations* to which the patient was also habitually subject. E. A. Cockayne noted the liability to sprains, and in explanation thereof suggested that all the fibrous structures around the joints were unduly weak and thin in these cases. He also commented upon the small physique of the patients, a point previously mentioned by Harman.

Van der Hoeve and de Kleijn were the first to notice *otosclerosis* in connection with this very interesting anomaly. Out of 11 without blue sclerotics, all were deaf and ten had broken one or more bones. In their second family three members were deaf from otosclerosis.

Van der Hoeve says that the blue sclera is easily observed; the fragility of the bones, on the contrary, can be present unobserved because an accident is necessary to put it in evidence, and deafness is progressive, so that it is not perceived before a certain age—so although all the symptoms of the syndrome may be present only the blue scleras are noticed.

DISEASES OF THE CORNEA

The more interesting part of the external fibrous coat of the eye-ball is the glass-like cornea, which, in the adult, makes up about one-sixth of the whole tunic. At birth it constitutes about one-fifth of the circumference of the globe. Viewed from the side, it is easy to demonstrate the fact that it forms a segment of a smaller circle superimposed upon the surface of a larger one. The radius of curvature for the central one-third of the anterior surface is 7.8 mm.

The normal cornea is not absolutely circular, being 12 mm. in its horizontal, and 11 mm. in its vertical, diameter. It weighs 180 mg. It is thin in the center (0.8 mm.) and comparatively thick (1.10 mm.) at its junction (*limbus corneæ*) with the sclera (margin of the *foramen scleræ anterius*). In the latter situation, the white sclerotic coat overlaps the transparent cornea; the inner, concave surface of the latter is greater than the outer convex surface, producing a bevelled effect. In other words, the cornea extends, to a slight degree, beneath the sclera, being partially hidden by the opaque, white, tissue with which it is intimately blended. It is attached to its scleral border much as a watch-glass is set into its case. In the newborn, this does not hold true, for here the corneal margin seems to occupy a groove in the scleral substance.

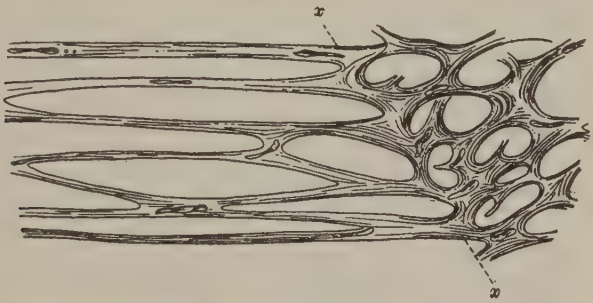

Fig. 103.—The limbus corneæ, showing the oblique union with the fibers of the sclerotic. (American Encyclopedia of Ophthalmology, Vol. i.)

The stroma of the cornea and Descemet's membrane become continuous with the iris at its angle, by means of the meshwork of the iris angle, which will receive separate consideration.

The cornea attains its full growth early in life, and, unless the eye be attacked by some intrauterine or infantile disease that stretches the eye-coats, such as buphthalmus (congenital glaucoma), its diameters are not much affected by subsequent diseases. This is why the stretching of the tunics in axial myopia, and in the various forms of adult glaucoma, acts chiefly on the posterior segment of the eye-ball.

The composition of the cornea and sclera is very similar; it is chiefly the arrangement of the fibers that makes the one transparent and the other opaque. The *substantia propria* of both is made up of closely-woven bundles of connective tissue fibers arranged in layers.

The cornea is arranged in five layers, or laminæ, *viz.*, the anterior epithelial layer; Bowman's membrane; the substnatia propria; Descement's membrane; and an endothelial layer.

The anterior lamina consists of from 5 to 10 layers of epithelium, continuous, and almost identical with the epithelium of the conjunctiva covering the globe. This is the only layer of the cornea which is regenerated after having been destroyed. The cells lying next to Bowman's membrane are cylindrical in shape, becoming more and more flattened as they approach the external surface, where they are seen as stratified pavement epithelial cells. The arrangement of this epithelium is the most regular of any in the human body, and neces-

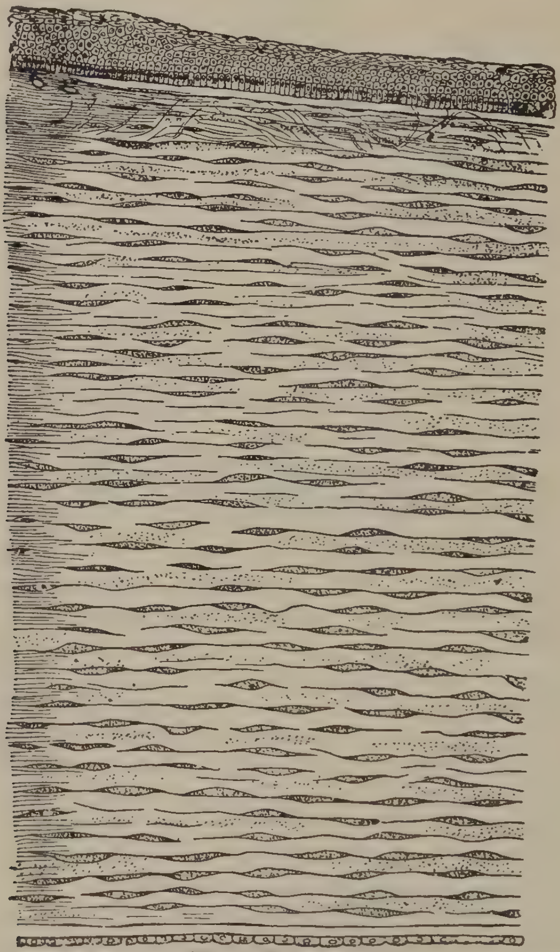

Fig. 104.—Section of the cornea showing five layers. (American Encyclopedia of Ophthalmology, Vol. i.)

sarily so, in view of the function of the cornea as a part of the optic system.

Congenital Anomalies of the Cornea.—These are numerous but rare. Among them may be mentioned *congenital staphyloma, congenital opacities* and vascularization of the cornea, due to either developmental defects, ocular injuries during parturition or to keratitis *in utero*. The *large cornea* in *congenital glaucoma* (buphthalmos) is brought about by developmental defects of the ligamentum and the canal of Schlemm. Congenital anterior staphyloma, opacities and vascularity of the cornea are, according to Treacher Collins, due to "atypical development of the mesoblast intruding between the surface epithelium and lens vesicle." Congenital opacities and vascularization of the cornea frequently co-exist. It is notable that congenital opacities are not attended by any excavation or facet.

Congenital corneal opacities are usually present in microphthalmos and congenital anterior staphyloma. Viewed in microscopical section, the cornea shows absence of the anterior limiting membrane, departures from the normal of the fibrous tissue lamellæ of the parenchyma and the presence of deep blood-vessels. We occasionally meet with congenital opacities which are more or less colored.

Sclerophthalmos is a congenital corneal abnormality in which the corneal margin is obscured by a dense white opacity characterized by its similarity to that of the sclera, occupying a part or a whole of the circumference of the cornea. *Arcus juvenilis* (*embryotoxon*) is another congenital marginal opacity which has the form of a complete ring free from vascularity and differing from *arcus senilis* (*gerontoxon*) in that there is no diaphanous zone between the opacity and the margin of the cornea. Corneal opacities are frequently associated with other anatomical defects in the configuration of the cornea.

Congenital ectasiæ have been reported by Pincus, Würdemann, and others. Pincus ascribes his case to an inflammatory condition active in the second half of fetal life. In Würdemann's case, the protrusion was 5 mm. high and 7 mm. in width, with no disturbance of transparency, a feature which makes the case unique.

Microcornea is always present in cases of microphthalmos. Fuchs has observed that in many cases of inherited lues, the cornea assumes the form of a vertical ellipse.

Congenital ectasia is probably due to a delayed development in the fetal cleft forming a *coloboma* of the cornea, which later becomes filled with corneal tissue, varying greatly from the normal, which is formed during the later weeks of intra-uterine life.

Phlyctenular Keratitis. Vascular Keratitis. Phlyctenular Ophthalmia. Fascicular Keratitis. Lymphatic Keratitis. Strumous Ophthalmia. Scrofulous Keratitis. Pustular Keratitis. Phlyctenular Keratoconjunctivitis. Eczematous Keratitis. Tubercular Keratitis.—A prevalent corneal affection, usually an extension of the same form of conjunctivitis, characterized by the appearance of small, single or multiple nodular lesions on some portion of the cornea, the limbic area being the most frequently involved.

As early as 1869 Iwanoff correctly recognized a protuberant cellular infiltration of the epithelial layer resting on Bowman's membrane. These nodules are readily identified by their clinical features alone. At the beginning, they are observed as small, translucent projections, restricted to the epithelial layer and resting on Bowman's membrane. Later they break down, become yellowish in color and small ulcers are formed. Ordinarily the ulcer thus formed is shallow and, as there is little loss of substance, the remaining opacity is faint. In other cases the disease displays a migratory tendency and extends farther into the cornea, either along its surface or, in severe cases, into its depth, when the breaking down and destruction is so extensive as to eventuate in perforation. In these severe cases, exudate from the onset is discernible in the deep layers of the cornea as a diffused infiltration, the overlying epithelium being stippled. The surface extension of the ulceration, in some cases, assumes serpentiform characteristics and displays clinical features akin to fascicular keratitis. The condition occasionally assumes the clinical aspect of a pannus (*pannus eczematosus*), when new formations of tissue and blood-vessels develop in any portion of the cornea, differing, in this respect, from trachomatuos pannus which has a predilection for the upper part of the cornea, is thicker, more vascular and apt to be permanent, while that of eczematous origin usually disappears without any remaining trace.

Instead of being vesicular, as the name phlyctenule implies, the nodules are solid formations, consisting chiefly of an accumulation of leukocytes.

In rare instances the nodules have been found to involve Bowman's membrane.

With reference to *atypical cases*, Parsons* says that Bass found nodules below Bowman's membrane in a case of prolonged scrofulous keratitis with superficial opacities. The nodules consisted of new-formed fibrous tissue, with flattened nuclei lying parallel to the surface; they involved either the whole or only the deeper part of Bowman's membrane, having either a broad basis of attachment to the substantia propria or a narrow pedicle.

Gifford, in 1886, ascertained the consistent presence of staphylococci (*aureus* and *albus*) in the conjunctival secretions or pustules surrounding the eye, in cases of keratitis phlyctenularis. In 28 cases these bacteria were found in 26. With reference to the bacteriology of this disease Parsons thinks that most late observers have found staphylococci, which may be accessory, though not causal, but are more likely to be mere contaminations.

Phlyctenular keratitis is most commonly observed in children, between the ages of 2 and 12 years. It is rare before the second year of life, but occasionally occurs after puberty. Those afflicted with this form of keratitis frequently suffer from rhinitis, eczema of face and scalp, hypertrophied tonsils and adenoids, and glandular enlargement.

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* Pathology of the Eye.

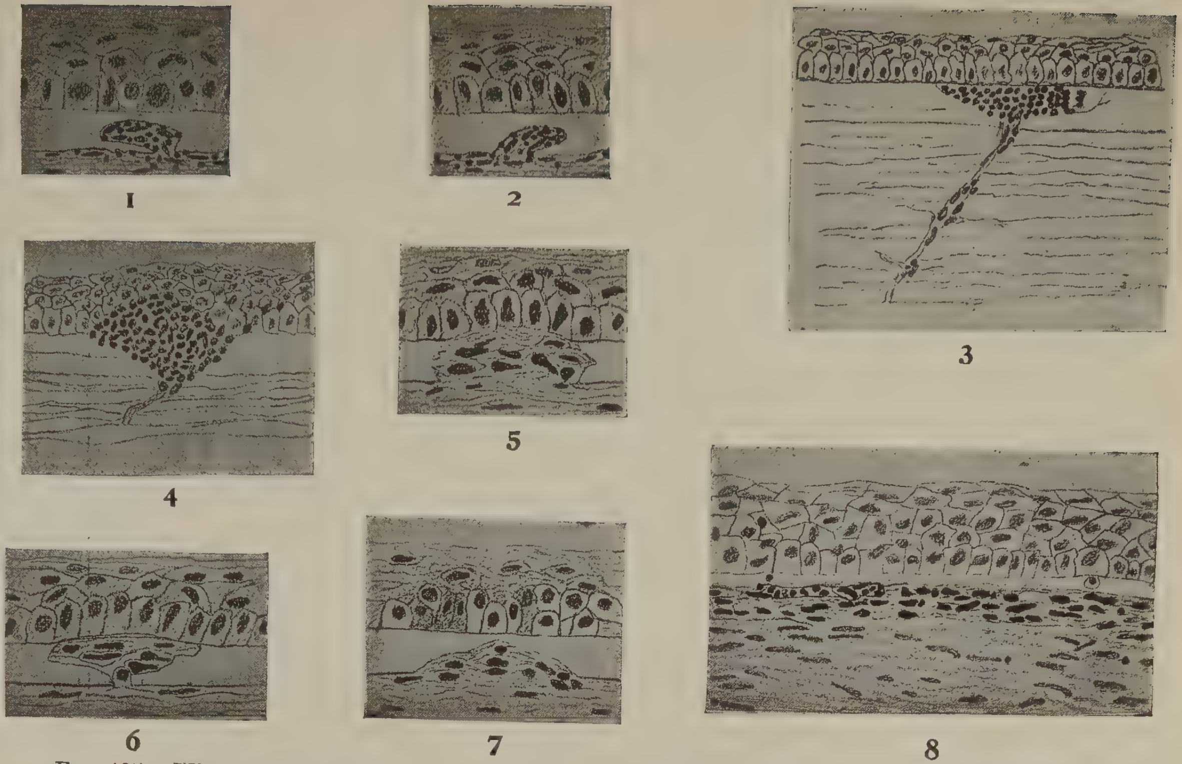

Fig. 105.—Microscopical sections of phlyctenules of the cornea. Showing 1, and 2, beginning phlyctenule; 3, and 4, developed phlyctenule; 5, 6 and 7, scar following the healing of a phlyctenule; 8, phlyctenular pannus. (After Baas.)

Many of these children manifest signs of the "exudative diathesis" of Czerny.

The observations of Hayashi, resulting from a study of the pathologic anatomy of five corneal and three conjunctival phlyctenulæ, showed that the most pronounced early changes are to be found in the most superficial layers of the substantia propria, and that they are present when the epithelium and Bowman's membrane are yet unaffected. These layers, however, do not long escape involvement; the epithelium is soon raised from Bowman's membrane and leukocytes (occasionally a few lymphocytes) and fixed corneal cells make their appearance between those layers of the corneal parenchyma nearest the lesion.

Symptoms.—Photophobia, frequently intense, and *blepharospasm,* not commensurate with the corneal involvement, and profuse lacrimation are characteristic of this affection.

Etiology.—Considerable diversity of opinion exists regarding the etiology of phlyctenular keratitis. Late observations leave little to support the ectogenous bacterial theory and have added most convincing proof of its endogenous origin, *i.e.*, that the changes are produced mostly by the action of the toxins of tubercle bacilli or bacillary fragments, often associated with lesions due to secondary infections. Straub's investigations have proved that "scrofulous" (*i.e.*, tuberculous) children have practically the same specific weight as water, that of the normal child being greater. These observations definitely prove that there is a consistent variation in their bone densities, the normal child having a greater deposit of lime salts.

Bruns is inclined to discard all other etiologic theories of phlyctenular ophthalmia in favor of a neuropathic phenomenon which he believes is induced by auto-intoxication. He offers the following observations as a logical basis for his views: "Auto-intoxication, originating in the great majority of cases, as the effective treatment clearly shows, in derangement of the gastro-intestinal function; not all persons being equally liable to these morbid processes, but much more particularly those in whom we recognize clinically the scrofulous, lymphatic or exudative diathesis; such persons being especially liable to tuberculosis and to other infectious diseases, which in their turn further depress the metabolic and catabolic pocesses, the functions of digestion, assimilation, secretion and excretion, and these intensify and perpetuate the state of auto-intoxication." These views are not, of course, inconsistent with the theory that tubercle is the essential element in the disease.

Colombo* also believes that the causal factor in phyctenular ophthalmia is to be found in auto-intoxication when the poisons, originating mainly in the intestinal tract, reach a state of concentration sufficiently high to impair the bodily resistive forces. In a series of 115 cases, indican was present in variable amounts in 82.6 per cent., and in the remaining 17.4 per cent. he found traces or none at all.

* Klin. Monatsbl. f. Augen., l., pt. II (1912), p. 610.

Malnutrition, in this, as in many other diseases, surely has a predisposing influence by lowering the body resistance, but, since few ill-nourished children become affected, it cannot be regarded as more than a predisposing factor.

Burnett, in a broad sense, holds the same opinion as Bruns, who rejects the tuberculous theory on the ground that since from 10 to 12 per cent. of examined cases gave negative von Pirquet reactions, the theory had failed, a contention which is not acceptable, as every clinician recognizes the fact that there are many persons who are unmistakably tuberculous or luetic who do not react to the von Pirquet test for tuberculosis or give a positive Wassermann reaction for lues.

Derby and Ayers have contributed valuable evidence to establish the relation between recurrent superficial keratitis and tuberculosis. The ages of the patients averaged 9½ years; family history of tuberculosis was positive in 25 per cent.; temperature elevated in 48 per cent.; positive signs of tuberculosis elsewhere in the body in 44 per cent.; positive cutaneous reaction in 92 per cent. In commenting upon the cutaneous test, these investigators regard a negative reaction of greater diagnostic value than a positive one, since the reaction in so many individuals is positive.

In 58 children, suffering from phlyctenular ophthalmia, Weekers obtained a positive von Pirquet reaction in 51; in the remaining seven the reaction was either doubtful or negative. In 123 adults having phlyctenular disease, Cohen found incipient tuberculosis in 12 per cent., florid phthisis in 3 per cent. and in 52 per cent. there was a family history, or a suggestive history, of tuberculosis. These statistics were compiled prior to the discovery of the von Pirquet test, which explains the low percentage obtained by the earlier investigators.

Verhoeff believes the phlyctenule to be an anaphylactic phenomenon. His theory is that the tissues become sensitized by previous infection so that a slight re-inoculation is sufficient to cause a reaction.

Davis and Vaughn* studied 40 cases (using the von Pirquet test diagnostically) ranging in age from seven months to 47 years (average age, about 11 years). They observed the following: 28 (70 per cent.) gave a positive reaction, while in 12 (30 per cent.) the test was negative; an elevated temperature occurred in 19 cases (47.50 per cent.) and reduced in three (7.50 per cent.) and unaffected in 18 (45 per cent.). There was a focal reaction in the eyes of three patients. They say that whether the phlyctenule itself, which may be considered a "pseudo-tubercle," is due to tubercle bacilli, or to the toxins of this bacillus, or to another cause, is yet to be determined. In the meantime, judging from their limited use of tuberculin in these cases, they conclude that tuberculin should be used in every case, both as a diagnostic and as a therapeutic measure, and that general hygienic and diabetic measures should be carried out just as in any other disease in which the system is in a run-down condition.

* Ophth. Record, xxi, No. 9 (September, 1912).

Stephenson* believes that while nobody asserts that the phlyctenule itself is of tuberculous histologic structure, or that it contains tubercle bacilli, nevertheless it is most ordinarily held that the characteristic lesion occurs only in those who are subjects of tuberculosis, latent or otherwise

Walter† draws our attention to two possibilities that may explain the negative finding of tubercle bacilli in these lesions: (*a*) Imperfection in staining technique; (*b*) their quick destruction after infection. He adds that Wegelin, in a study of (supposed) healed calcareous tuberculous lesions, was able to demonstrate tubercle bacilli of low virulence by a special process of staining, namely, the alkaline hypochlorite method, so that it remains to be seen whether one might not more often demonstrate tubercle bacilli in these lesions by employing more appropriate methods of staining. The conclusion, he thinks, is also justified by this and by the work of Rabinowitsch and Schmitz that the tubercle bacilli in most of the so-called healed tuberculous lesions, even the calcareous or encapsulated ones, are still viable.

Diagnostically it is probably preferable in this disease to first apply the von Pirquet test; if negative, the intradermal method may then be used, the latter being more definite in its results. It is generally conceded that a local, focal reaction must be obtained for a decisive diagnosis.

Treatment.—Sufferers from phlyctenular keratitis should, when expedient, be placed in the best possible hygienic surroundings, and should have fresh air and nourishing, bland diet. Fats, sugars, acids, tea and coffee should be, withdrawn from the dietary. Cryptic or hypertrophied tonsils and adenoids should be removed. Nasal catarrh, so commonly associated with this disease, responds readily to warm irrigations of Dobell's solution, followed by applications of one of the mercurial ointments. Locally, no remedy is more efficacious than yellow oxid of mercury, which should be applied once or twice daily in strengths of from 2 to 5 per cent. Holocain is a valuable remedy for the control of pain, while atropin acts efficacrouly in combating certain complications of the disease.

Bruns regards the internal administration of mercuric bichlorid as almost a specific for this affection. Gradle has used anti-staphylococci vaccin with satisfactory results, when staphylococci were present in the secretions. Coleman has produced cures by *x*-ray treatment in cases which resisted all other therapy.

When tuberculin is exhibited therapeutically, either old tuberculin (T. R.) or the emulsion (T. E.) administered hypodermically, preferably in small doses, every three to eight days. Wright's principle, based fundamentally on the stimulation of antibody-formation, suggests the propriety of infinitesimal doses. This reasoning, and the probable harmful effect of physiologic doses, has lead a majority of clinicians to abandon the method of von Hippel—that of rapidly increasing the dosage, governed by the temperature.

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* British Med. Jour. (Apr. 16, 1910).

† Jour. A. M. A., lxi, No. 13 (Sept. 27, 1913).

Corneal ulcer—of which there are many varieties—presents much the same aspects as the same disease in the adult, and there is, consequently, no justification for special treatment of the subject in this chapter. However, as one of the most important sequels of ulcerative keratitis, it may be said that the *clearing of corneal cicatrices* is greatly influenced by the extent of the ulcerative process and the age of the individual. Circumscribed and superficial cicatricial deposits undergo greater absorption than those which are deep and diffuse. Owing to the softness of the corneal tissues and the active lymph circulation therein, *corneal cicatrices in young subjects are more readily absorbed* than are the corneal scars of adults. However, cicatrices due to corneal perforation of all sizes remain practically unchanged at all ages. The methods to be employed in the treatment of corneal scars in children should be left entirely to the trained ophthalmologist.

Transplantation of the Cornea.—As this operation is most commonly indicated in juvenile subjects, for the relief of blindness due, in most instances, to *opaque corneæ following ophthalmia neonatorum*, it may be stated that great encouragement has in late years been derived from recent observations and experiment. These have taken the form of transplanting human corneal tissues instead of animal corneæ. In the latter case it generally happens that even after a successful transplantation the graft becomes almost as opaque as the scar tissue it was intended to replace.

Magitot* reports a case in which a boy of 14, with a cornea almost entirely opaque, had a rectangular window made in the opaque tissue 4 by 5 mm. in size, extending down almost to Descemet's membrane. In this window was fitted a graft from the cornea of an eye enucleated eight days previously for absolute glaucoma. At the time of enucleation the cornea had been steamy, but it cleared up in a few hours after being placed in the preserving fluid. When the bandage was removed on the third day the graft was transparent and fluorescein did not stain at any point. Eight days afterward the eye was left uncovered, and the fundus reflex could be seen through the new window. Irregular astigmatism was present but gradually diminished. At the end of a year the boy had vision of 1/7 through the corneal window. His vision before the transplantation had been 1/17, through a peripheral optical iridectomy. Magitot suggests that this method can be employed to utilize, for purposes of transplantation, the corneas of stillborn children; and he calls special attention to this successful use of a cornea apparently damaged by high intraocular tension.

Lohlein† has also reported a case in which he transplanted a corneal segment from one human eye to another. The visual result, one year after operation, was 3/18 vision with −1.00 D. sphere.

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* Jour. Am. Med. Assocn. (1911), p. 18; and Archives d'Ophthalm., xxxii (1911), p. 361.

† Arch. of Ophthal. (May, 1912).

His last observation records the eye as white and not irritated; no photophobia present; the corneal flaps unchanged and its sensibility somewhat less than that of the rest of the cornea.

Parenchymatous Keratitis.—This is one of the most important diseases of childhood and calls for extended notice. It is also known as anterior uveitis, as well as *interstitial, inherited, luetic, strumous or diffuse keratitis,* and is essentially an affection of the corneal substantia propria. It is characterized by a leukocyte infiltration of the corneal parenchyma, generally beginning either at the center of the cornea and spreading outward or showing itself first at the periphery and advancing towards the center. When the infiltration is complete the whole cornea has a "ground glass" appearance, and vision is reduced to the perception of shadows or finger-counting. We see blood-vessels running from the corneal limbus, branching in the deeper layers as they approach the corneal center. If a plus 20 spherical lens be used as a magnifier and placed behind the concave mirror of the ophthalmoscope numerous spots and streaks are revealed in the corneal substance.

Regression of the corneal lesion always begins at the sclerocorneal junction, so that the important corneal area opposite the pupil clears last. This circumstance postpones the return of vision even when clearing of the infiltrate has taken place almost in its entirety. Some of the opacity always remains but as a rule useful eye-sight is obtained after many weeks or months of waiting. Rarely the cornea does not clear up and the disease takes on a condition of *corneal sclerosis.* Whatever happens, years after the attack or attacks the remains of empty blood-vessels and infiltrates can be seen with the ophthalmoscope even in corneæ that appear to be quite transparent and when tests show normal or nearly normal vision.

When the disease advances by the marked formation of capillaries there appears a uniform, pale-red, vascular area commonly known as "salmon patch." The amount of vascularity is usually in keeping with the density and area of the infiltration. In severe and rather acute cases the entire cornea has a reddish appearance while many cases show relatively little injection. Hence the two forms of the disease, the *vascular* and the *non-vascular.* Now and then, especially in the latter case, the disease lasts a comparatively short time and the corneal deposits clear up in a few weeks, but as a rule the affection is a very chronic one with symptoms showing themselves for several months. It must always be remembered, however, that unless the deeper tissues of the eye are destroyed (by choroiditis, retinitis, etc.) even a marble-white cornea may clear up and good vision be restored after a number of months of suffering.

An important fact, ever to be borne in mind, is that behind the affected cornea some form of *uveitis* may be progressing that constitues the real menace to eye-sight and presents a serious bar to complete recovery.

Both eyes are usually involved, and there may be long intervals between the attacks, so that the duration of the disease as a whole may cover several years.

The *prospects for vision* are most favorable in quite young subjects; indeed the earlier in life the disease the sooner it seems to regress and the less likely is the patient to have damaged eye-sight from deep infiltrations, destructive uveitis and retinal infection.

It was von Hippel who first (1908) found the *spirochœta pallida* in corneal scraping from a case of interstitial keratitis and thus established the leutic origin of the disease. Later it was found that the Wassermann reaction was decidedly positive in about 85 per cent. of the cases; about which time it was also established that various forms of corneal trauma often acted as the predisposing cause of the infiltration.

Hutchinson teeth and other stigmata of *inherited syphilis* are almost invariably present in children suffering from this chronic disease. Fournier also noticed that persistence of the first teeth was a common occurrence in parenchymatous keratitis. Many authors have noted the defects in nutrition that are so often associated with luetic keratitis but this, perhaps, is merely a part of the inherited syphilis.

In the *treatment* of this disease little can be done that is of local importance unless the attack be acute or unless *iritis* or other form of *uveitis* is present, in which case the remedies proper to these diseases should be given—as detailed under "Diseases of the Uveal Tract." Atropin is very useful in combating iritis or iridocyclitis and in preventing the ruinous sequels. Dionin (5 per cent.) solution applied two or three times daily relieves pain and photophobia. Dark glasses and eye-shades add to the patient's comfort, protecting the sensitive eyes from light. Hot compresses, or bathing the eyes with *very hot water*, is a remedy of great value. When a luetic origin has been established an anti-syphilitic course should be prescribed, bearing in mind, however, that the disease is hereditary in character and that hygienic measures—fresh air, good food, regulation of the bowels, etc.—play quite as important a rôle as arsphenamin and similar drugs. Stephenson is in favor of atoxyl given in conjunction with mercury. He uses the intramuscular injection of 0.25 to 0.50 gm. about once a week—more frequently if the disease is very active. Not more than 6 gm. should be given in all.

In some cases arsphenamin (salvarsan) has produced brilliant results and this remedy should in most cases be given a trial in conjunction with the topical applications and hygienic care above detailed. However, the pediatrist must not be discouraged if he finds the corneal infiltration deepen and spread *pari passu* for several weeks in spite of the most conscientious care. The element of time is of great importance in this essentially chronic and obstinate disease. However, with patience and perseverance in the course of conduct laid down even the most unpromising cases do well and after months of disability the youthful patient usually gets well, with restored eyesight.

DISEASES OF THE UVEAL TRACT

The uveal tract, or *uvea*, comprises the *chorioid* (*choroid*), the *ciliary body*, the *ciliary processes*, and the *iris*. This collection of pigmented and highly vascular tissues forms, anatomically, physiologically, and pathologically, a rather definite section of the intra-ocular apparatus. It derives its name from the fact that when the outer covering, composed of the cornea and sclera, is removed from the globe, a middle coat is exposed that closely resembles a purple (uvea) grape. The anterior segment of the uvea is composed of the iris, pierced by the pupil. The iridic tissue extends to the sclero-corneal junction, where it is continued inward as the ciliary body, a meridional, circular organ, that still farther backward sends out ciliary processes and joins the choroid, which, in its turn, lines the ocular interior back to the optic nerve entrance.

The whole tract is soft and readily breaks down. The choroidal elements are composed chiefly of connective tissue, bearing blood-vessels and lymph spaces, indented to afford nourishment to most of the organs within the eye-ball. The ciliary body is made up of the muscle that regulates the focusing apparatus (accommodation) of the eye, as well as of numerous vascular and nervous bundles that are concerned in intra-ocular secretion and excretion. These constituent organs will be considered separately.

The *iris*, which is continuous with the choroid, is a circular, colored curtain, or diaphragm, lying in front of the lens. It has a round opening of varying width—the *pupil*—which lies slightly to the nasal side of the center, and acts chiefly as a regulator of the amount of light admitted into the interior of the eye; in conjunction with the other parts of the dioptric apparatus, it assists in giving sharp definition to fundus pictures. It separates the anterior from the posterior aqueous chamber. The pupillary margin of the iris is bevelled at the expense of the outer surface, and is finely crenated. Until the seventh month of fetal life the pupil is closed by a thin, semi-transparent membrane, which occasionally persists, in part or in whole, after birth, under the name of *persistent pupillary membrane*. When the iris is contracted its pupillary margin rests lightly on the anterior surface of the lens. At its periphery, or root, at the sclerocorneal junction, it turns abruptly backward and becomes continuous with the ciliary body; this is called the ciliary border. The diameter of this border is 12 mm. and does not vary. When the pupil is dilated the iris hangs (or floats) free in the aqueous humor, and does not touch the lens. The average width of the pupil is 4 mm.; a slight difference in the size of the pupils is not necessarily pathologic. The thickness of the iris varies; when contracted it measures 0.3 mm., when dilated 0.75 mm. The point of minimum thickness is at the ciliary border, where it measures 0.2 mm.

Seen from in front, the iris presents a great number of patterns, as well as all sorts of colors, from light-blue to deep-brown, the variation in color being due chiefly to the differing quantity and arrangement of the dull-brown pigment deposited on its anterior surface and viewed through the corneal and aqueous media.

In *albinos* pigment is lacking, not only in the stroma of the iris, but in all other portions of the uveal tract as well; in negroes, the amount is relatively large. The ultimate pigment deposit, whether large or small in amount, does not appear until after birth; hence *all babies have light blue eyes for the first few weeks of life.* Irregularities may occur in this deposit, so that an iris may be partly blue and partly brown (*heterochromia*). When this happens the parents are generally of different complexions.

Contraction of the pupil is brought about by the sphincter pupillæ muscle, a narrow band of fibers about 0.9 mm. broad, which encircles the iris near the free border of the pupil. This muscle is supplied by branches of the third (oculomotorius) nerve.

Dilatation of the pupil is accomplished by relaxation of the sphincter pupillæ, contraction of the muscular coat of the iridic arteries, and by contraction of an irregular layer of unstriped muscle fibers called the dilator pupillæ, derived from the *stratum pigmenti.* These fibers radiate from the margin of the pupil to the ciliary body. The last two sets of muscle fibers are controlled by the sympathetic.

The Iris and Its Diseases in Childhood.—Anomalies of the Pupil.—The bluish coloration of all infantile irides has already been referred to. Harman* observed the pigment in the irides of children, the offspring of a blue-eyed, fair-haired father and a brown-eyed dark-haired mother. At birth, in each case, the irides were of the usual dull slatey-blue color, and the iris tissues were obscured as though coated with some fine-textured material. Clearing of the iris stroma was noted from the third to the sixth week of life. Two children developed blue eyes, one blue with a suggestion of violet, due to rims of finer dark stroma at the margins. The other blue became bright and cold in tint, owing to a marked thickening of the stroma in the intermediate zone. Two children developed brown irides. The first sign of brown pigment was noted at the sixth week. The pigment was in broad irregular patches extending from the basal margin. The development was earliest in the temporal half of the iris. The patches extended and fused until the whole was brown. The tint became full and pure in one child; in the other there remained at the age of two years some suggestion of bluish or greenish tint in the depth of the crypts of the iris.

Congenital Anomalies of the Iris and Pupil.—One of the best known of the latter is *persistent pupillary membrane.* The persistence of part of the fetal pupillary membrane while not a common condition is relatively rare. Statistics vary widely, as shown by the reports of Mooren, 14 in 100,000; Uhthoff, 6 in 10,000; Königstein, 21 in 3000 patients; Schleich, 13 in 150; Franke, 32 in 3508; Stephenson, vestiges in 68 of 3414. Such a variation is no doubt due to the varied classification of different authors. Where the merest vestiges are recorded the ratio will of necessity run higher. The pupillary membrane being a structure normal to fetal life, it is not surprising that the ratio of positive finding runs high in newborn children, and this coupled with the fact that in later life the ratio is lower inevitably leads one to conclude

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* Trans. Ophth. Soc. Unit. King., xxxiv, p. 137.

that the pupillary membrane may disappear not before, but some time after birth. In the latter part of the second month of fetal life the optic vesicle is differentiated into the anterior or iridic part, a middle or ciliary part, and a posterior or retinal part. It is in the iridic or anterior part that the changes relative to the present subject take place. The anterior chamber is formed not as often supposed between the iris and the cornea but between the cornea and the vasculopupillary membrane. The mesoblastic tissue, growing in from all sides in the anterior part of the eye, causes the thin iridic segment of the optic vesicle to bend over the equator of the lens and develop inwards towards the pupillary region. This mesoblast, the forerunner of the iris stroma, thus carries upon its posterior surface the iridic portion of the optic cup, their development going forward hand in hand. The stroma of the iris, the pupillary membrane and the cornea are all mesoblastic tissues. The lens, early formed, is at first in contact with the cornea, but becomes separated from it by the differentiation of the pupillary membrane and iris stroma. By the fourth month the iris is formed and the anterior chamber is lined with endothelium. The pupillary membrane persists until the seventh month, at which time it begins to be absorbed and at birth it should have completely disappeared. The anterior vascular sheath has a vascular connection with the posterior lens sheath, but in all other respects they are distinct structures; hence one may disappear while the other persists.

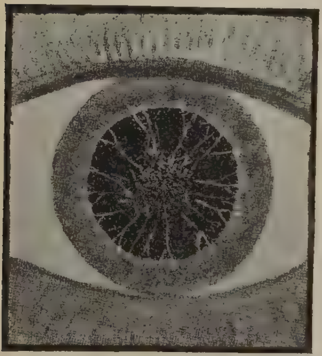

FIG. 106.—Persistent pupillary membrane. (After Massey.)

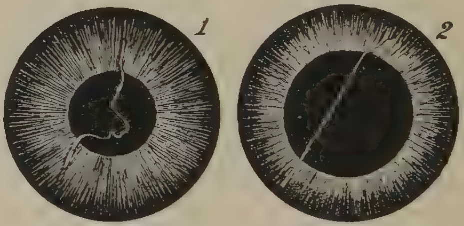

FIG. 107.—Persisting pupillary membrane. 1, Pupil contracted; 2, pupil dilated. (Wickerkiewicz.)

As usually observed the *persistent pupillary membrane* varies in color, in extent and in its relation to surrounding parts. Persistent remains are distinguished from posterior synechiæ by their taking origin from the anterior surface of the iris, usually in the region of the smaller circle, never from the pupillary margin and frequently much farther peripherally than the smaller circle. The latter fibers may even spring from the ciliary border of the iris, join together with their ends falling free in the pupillary area, or matting together into a sort of network from a central plaque of light color. This plaque may exist free in front of the lens capsule or be adherent to it. The pupillary fibers are generally considerably lighter than the iris, but often in their color and whole appearance they resemble the iris stroma. The movements of the iris behind the persistent membrane as a rule are unimpeded. The lens is normal and clear except in a few instances where pyramidal cataract has been observed. Occasionally a central group of fine brown dots is seen upon the lens capsule. The condition is more often met with unilaterally. Very seldom is a simultaneous persistence of the posterior vascular capsule seen. The arrangement of the fibers varies in different cases and shows changes in tenseness or laxity with dilatation or contraction of the pupil. The fibers have been seen disposed in the following manner: First, several fibers arising from the small circle at different points in its circumference stretch across the pupil from a delicate network in front of it. Second, fibers run tangentially between two points in the small circle of the iris. Third, all the toothed projections of the small circle are prolonged inward and project beyond the pupillary margin. Fourth, one or more fibers attached to the small circle of the iris float free at their other extremities. Fifth, a loop is formed by two fibers in front of the pupil. Sixth, one or more fibers arise from the iris and are attached to the lens capsule. Seventh, a fiber extends from the iris to the posterior corneal surface. Eighth, fibers unite in the pupillary region from a network more or less dense constituting a plaque, attached or unattached to the lens capsule.

Disturbance of vision as a rule is not observed except in those cases of a dense central plaque in which the disturbance may be so great as to necessitate operative interference.

In addition the pupil may show a number and variety of congenital abnormalities in regard to shape, size, position and number. When altered in position it is called *corectopia;* when in size, *microcoria* if small, *macrocoria* if large; when in shape, *discoria;* and when the number of openings is increased, *polycoria.* Corectopia and polycoria are considered under separate headings. Microcoria is occasionally seen where it is not the result of adhesions due to a fetal iritis. In such case it is generally associated with corectopia. Associated with congenital cataract a small immobile pupil is frequently seen which does not dilate well even when a mydriatic is used. Faulty shape, or discoria, where no tissue has been lost and the iris is intact, is met with both as a result of fetal iritis and also when no inflammation has taken place. At times the distortion is produced by the pull of a strand of persistent pupillary membrane, giving the margin of the pupil a toothed appearance, and the pupil itself a star-shape.

Aniridia is a condition of apparent complete absence of the iris. As a rule, however, tags or remnants of iris tissue are present, but escape detection clinically. It may be looked upon as a total coloboma of the iris. Almost without exception it is a bilateral condition.

A complete aniridia may exist in one eye, the other showing an incomplete absence.

Polycoria.—In this condition there are one or more supplementary pupils or openings in the iris; as many as 10 or more have been observed. But one opening, the true pupil, has a sphincter muscle; in the instances where clinically a widening or narrowing by the use of mydriatics or miotics was brought about, such movements were due to the changes in the shape of the true pupil and the adjacent iris, and not to the presence of accessory sphincters. The name polycoria is limited to actual holes in the iris. The division of the pupil by bands of persistent pupillary membrane and bridge colobomata are therefore excluded. Very rarely are two pupils of equal size seen. Rumschewitsch records a case showing 11 openings, and von Hippel one with 16.

Corectopia.—Here the normal pupil is not situated exactly in the center of the iris, and it is not unusual to find one or both pupils slightly eccentric, but a marked deviation constituting a clinical corectopia is rather a rare condition. The normal pupil is situated slightly in and up, directly in, or down and in. The latter is the most frequent. A displaced pupil is often small, inactive and not always completely circular. The dividing line between a normally eccentric pupil and one to which we apply the designation corectopia is of necessity not clean-cut. In well-defined cases the pupil lies so near the corneal margin that it is separated from it by but 1 or 2 mm. of of iris tissue. A classification of this anomaly has been made by Best. He divided it into four group. (1) The eccentric position of the pupil is the only anomaly. The other parts of the eye are normal, as is also the visual acuity. The direction of the ectopia shows no constancy. The condition is not rare. The pupil as a rule is elongated and oval, or with a more or less triangular or irregular form; it is surrounded by sphincter and reacts normally. In the iris there are no evidences of a former intra-uterine inflammation recog-

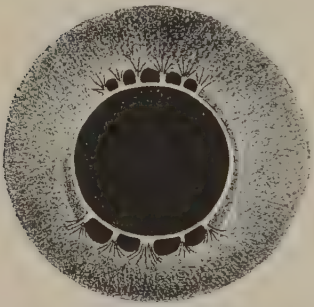

Fig. 108.—Polycoria with nine additional openings. (After Rumschewitsch.)

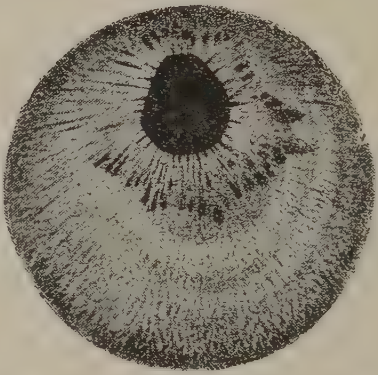

Fig. 109.—True corectopia. (Van Duyse.)

nizable. The condition is in the vast majority of the cases unilateral. (2) In this group, as Samelsohn early emphasized, the iris shows a dirty discoloration, and a decided change in its structure. The iris shows evidences of inflammation and is atrophied and irregularly pigmented. The pupil reacts badly or not at all. The iris border on the side of the deviation is atrophied in the pronounced cases, and the radial fibers, instead of converging towards the center of the pupil, converge towards the atrophied part, so that it resembles in appearance an iridectomy; in fact all variations in the shape of the pupil from a normal round one to an iris coloboma may exist. The occasional presence of a peripheral corneal scar arouses the suspicion of a possible perforation due to intra-uterine inflammation with a consequent iris prolapse and displacement of the pupil.

Coloboma of the Iris.—This striking anomaly, because of its being so very apparent, came early to the notice of ophthalmologists and descriptions of it were furnished by early writers. Coloboma of the iris may be met with as the only anomaly, or, as is frequently the case, other defects are present. Situated in the main downward, or downward and slightly inwards, it is called typical and is by far the commonest condition found. It consists of an absence of iris tissue ranging in the slightest forms from a mere nick in the pupillary border to a deficiency comprising one-sixth to one-third of the total area and reaching as far as the ciliary border. Incomplete forms are found in which the pigment layer alone is missing in a section corresponding to the site of the ordinary coloboma. This, when viewed superficially, is taken for a coloboma of the usual type, but upon closer inspection with oblique illumination its true character is recognized. Jackson reported a case where the left eye showed a slit extending downwards from the pupil less than 0.5 mm. wide, and looking like a streak of pigment or a large iris cleft. The ophthalmoscope proved it to be a true coloboma. It was separated from the normal pupil by a bridge of tissue 0.5 mm. wide. The movements of the iris and of the pupil were normal. By transillumination a coloboma 3 mm. wide was demonstrated and extended from the pupil to the ciliary region. Lens and choroid were normal. The coloboma involved chiefly the pigment layer. These are termed psuedo-colobomata.

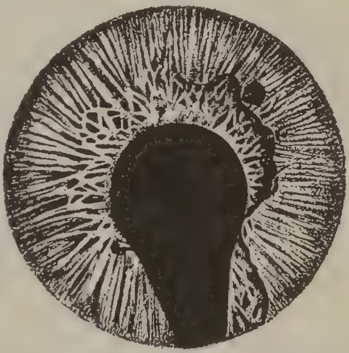

Fig. 110.—Typical coloboma of the iris. (After Seggel.)

Infantile Iritis.—Although infections of this membrane (*iritis*) are of great importance yet they are comparatively rare in children and when they do supervene demand the same treatment as adult iritides.

Distinctive, **acute diseases of the ciliary body** (*cyclitis*, for example) are not seen in children; nor are its congenital anomalies of sufficient importance to list here; and the same may with, perhaps, one or two exceptions, be said of the choroid (chorioid).

Coloboma of the choroid occurs as a not uncommon congenital defect in two forms—the *typical* and *atypical*. *Typical coloboma* of the choroid occurs at the lower part and, frequently, a little more to the nasal side. It is usually oval in shape, and may extend to or include the disc, though as a rule a bridge of choroid intervenes. Coloboma of the iris and other malformations frequently accompany it. Panas states that it is more common in the left eye than in the right and though generally binocular the left coloboma is larger. Examined with the ophthalmoscope the defective area appears glistening white, with an irregularly pigmented border. Retinal vessels are frequently seen crossing the area and occasionally a few larger ciliary vessels are seen at a deeper layer than the retinal. Pigment may invade the area to a more or less degree. The surface of the area is rarely smooth, but is marked with ridges and indentations. Fuchs, in giving the embryological cause, places the starting point at the fetal ocular cleft. This is found at the lower side of the secondary ocular vesicle and is designed for admission of blood-vessels into the interior. This cleft should close completely but the closure may be prevented if the mesoderm that conveys the blood-vessels does not undergo retrogression at the proper time. The layers of the ocular vesicles are separated and the interspace filled with mesodermal tissue. From this mesodermal structure fibrous tissue is formed which becomes ectatic from intra-ocular pressure. Thus the coloboma is primarily in the retina, and is analogous to what occurs normally in certain birds and animals. The pigment epithelial layer is absent over a part of the area, though often continued as an unpigmented row of cells before it ceases. The retina can be found in various degrees of attenuation and malnutrition. In some cases light perception may remain in the affected area. Defective vision is the rule in choroidal colobomata.

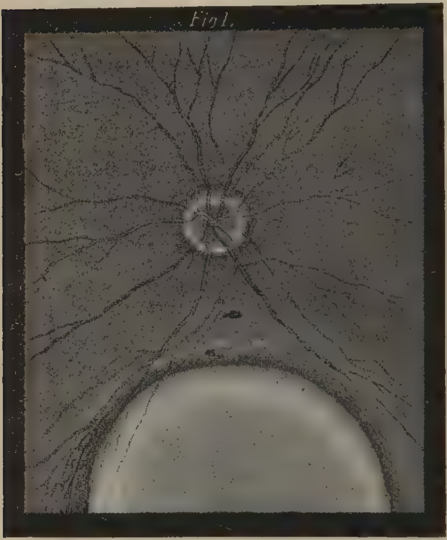

FIG. 111.—Coloboma of the choroid. (de Schweinitz.)

Atypical coloboma of the choroid is the name given to congenital defect in other parts of the choroid. Macular coloboma is the more common. Lindsay Johnson gives the name *extrapapillary coloboma* to the typical cases not involving the disc. The coloboma may be from the size of the optic disc to five times that dimension. It is round or oval and similar in appearance to the typical coloboma. It is often associated with other choroidal changes. Many regard the atypical type as the result of intrauterine inflammation.

Macular choroiditis, although often unrecognized until after puberty, is not uncommon in early life. It consists of an inflammation of and exudate into the macular region. It occurs in about 6 per cent. of all cases of myopia above 10 diopters. In about one-half of these instances both maculæ are affected. In children under 10 years of age this complication is rare, but it is quite common above 10, and in preference attacks the female sex in the proportion of three females to two males. As a rule it appears as a circumscribed plaque of a dull-red color, which eventually becomes white, edged with a pigmentary deposit. In some instances similar areas develop throughout the fundus, so that the ophthalmoscopic picture resembles the disseminated form of choroiditis. In 9 per cent. of the cases this condition is associated with vitreous disease, and in 10 per cent. with detachment of the retina. In a number of instances these central alterations are associated with hemorrhages, and in some they begin with bleeding in the foveal region. This *macular apoplexy* appears early as a blood-red spot which later on is absorbed, leaving several whitish eyelets and pigmentary accumulations. Owing chiefly to implication of the retinal elements the patient's vision is always lowered, although not so much, as a rule, as one would expect from the conditions revealed by the ophthalmoscope.

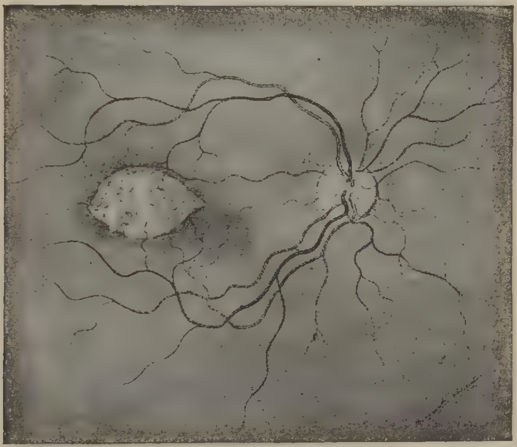

FIG. 112.—Macular coloboma of the choroid. (de Schweinitz.)

Syphilitic (disseminated) choroiditis is not infrequently the result of intra-uterine lues, or it may form a part of *parenchymatous keratitis* (*q.v.*), but its characters in childhood do not much differ from those of the adult forms.

Cataract in Infancy and Childhood.—That one may understand the exact meaning of cataract it is well to bear in mind the anatomy of the lens system, as depicted in the accompanying illustrations. The crystalline is a circular, biconvex, transparent, glass-like body, lying between the iris and the vitreous humor. It fits accurately into the shallow, saucer-shaped, patellar fossa of the vitreous, from which it is separated by the post-lenticular space of Berger. It is held in place by a *syspensory ligament*, the zonula (or zonule) of Zinn, and by the *ligamentum hyaloideo-capsulare.* The equator, or edge, of the lens, is about 1 mm. from the ciliary processes.

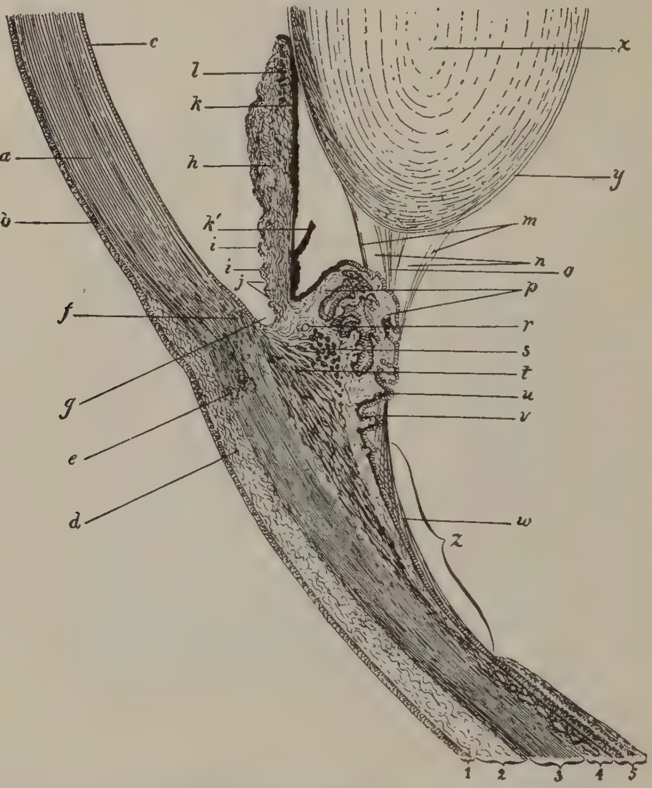

Fig. 113.—The immediate relations of the crystalline lens system. *a*, Cornea; *f*, canal of Schlemm; *g*, iridic angle; *h*, iris; *k*, posterior pigment layers (detached); *m*, *c*, zonular fibres; *n*, interfibrillar spaces; *p*, *r*, *s*, *t*, ciliary body; 1, 2, conjunctiva; 3, sclera; 4, choroid; *s*, retina. (After Quain.)

The lens is enclosed in a delicate, structureless, elastic envelope, lined in front by endothelial cells, which are wanting on the posterior surface. Owing to this and other differences, and, for the purpose of reference, this covering of the crystalline lens has been called the anterior and posterior capsule, although there is no distinct line of separation between them. The *capsule* is quite strong and elastic, though brittle. When cut through it tears irregularly, and the incised edges curl up in a roll with the inner surface outward. The minimum thickness of the capsule is at the posterior pole. Each surface shows a zone of maximum thickness occupying a position concentric with the equator toward the periphery of the lens.

The lens substance is formed by the invagination of the ectoderm, and is, consequently, an epithelial structure—the capsule being derived from the mesoderm. For this reason the lens grows (by conversion of the marginal cells of the anterior capsule into young lenticular fibers) larger, heavier, thicker, and harder, as age advances. Lens substance in process of formation can be found at all ages of life.

The hardening process begins in childhood, and affects chiefly the central portions, so that in the adult a distinct condensation of the tissues occurs, and a nucleus can be demonstrated.

Congenital Cataract.—It must be remembered that it is not easy to decide the ante- or post-natal character of any cataract and much has been written for and against the congenital theory of several of the cataracts included in Dor's table (Fig. 114).

In the *treatment of all forms of congenital cataract* Treacher Collins* advises us to wait until the child is 10 months old before operating. At an earlier age the cornea is so small and the anterior chamber so shallow that the necessary instrumentation cannot be as satisfactorily carried out as in a more fully developed eye. Moreover, the amount of aqueous humor is so small that it does not suffice for solution of the liberated lens substance. In some cases, in which the pupil is small and does not dilate well with atropin, it is best to do a preliminary iridectomy. In nearly all cases it is well to begin the cataract removal with a needling, for valuable information may thus be obtained as to the thickness of the capsule and the consistency of the lens, even should it fail to liberate much lens matter to the action of the aqueous. If the cataract is a dense, white, anterior polar one, set in a ring of clear, or partially clear, lens substance and apparently flattened from before backward, the so-called disc-shaped cataract, then an attempt should be made to separate the central white opacity with a needle and let it fall into the anterior chamber. Two needles are sometimes required to effect this. If, on pricking the capsule, milky-white fluid escapes into the anterior chamber (congenital Morgagnian cataract), it is well at once to evacuate this fluid, for fear of increased tension ensuing.

In some cases of congenital cataract, the whole lens and capsule can be removed in a most satisfactory way by forceps. Very often, however, such a procedure is followed by escape of vitreous. It is difficult to differentiate which cataracts can be safely dealt with in this manner. They generally seem to be complete cataracts with a tough capsule and lens matter of a gelatinous consistency.

If after a needling and some absorption of liberated lens matter, a dense, tough, white, fibrous-looking membrane remains, there is probably some atypical development of the anterior part of the vitreous. Under such circumstances an attempt had best be made forcibly to displace the membrane downward and backward out of the axis of vision. Of course the practical application of these rules should be left to the experienced ophthalmic surgeon.

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* Ophthalmoscope (September, 1908).

Juvenile cataracts, including the congenital forms, are generally *soft*, as opposed to the *hard* cataract of adult life. This one fact represents an important difference in their pathology and treatment and justifies a brief description of them here. If the lens be viewed by *focal illumination* (*q.v.*) through the dilated pupil and the opacity in the lens (constituting the cataract) shows striæ of an irregular, mottled appearance one has to deal with a *soft* cataract only. In

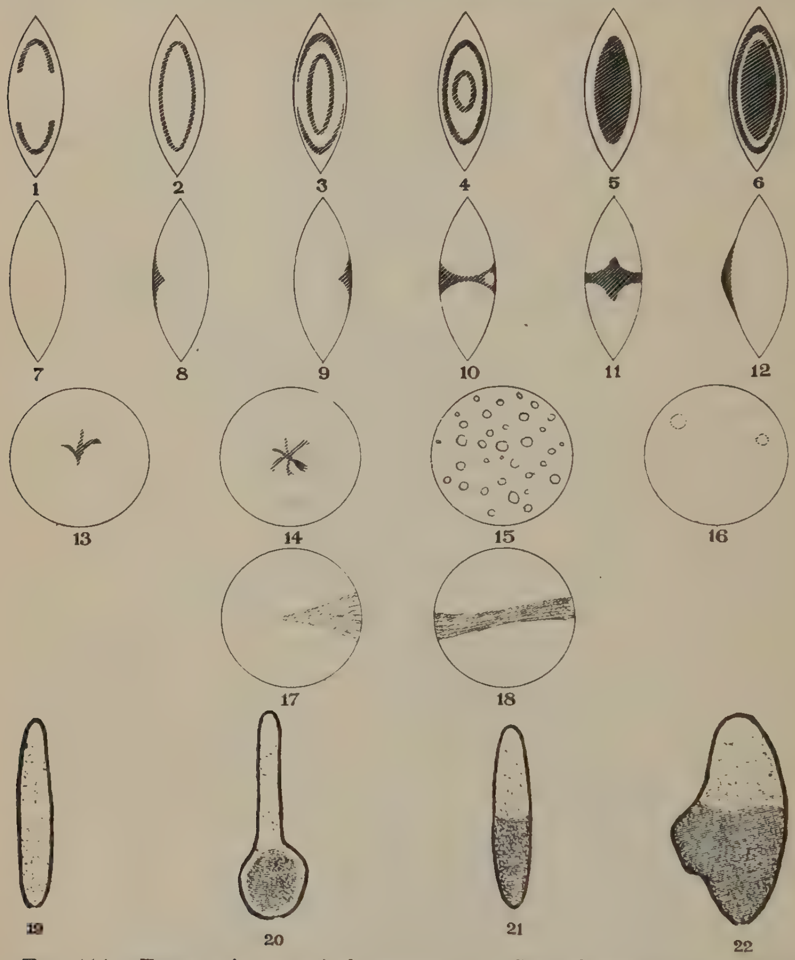

Fig. 114.—Forms of congenital cataract. 1, Partial zonular; 2, complete zonular; 3, partial double zonular; 4, complete double zonular; 5, zonular with opaque hard nucleus; 6, double zonular with total opacity; 7, central punctiform; 8, anterior polar; 9, posterior polar; 10, bipolar; 11, fusiform; 12, pyramidal; 13, 14, stellate; 15, punctate; 16, vesicular; 17, cuneiform; 18, bandlike; 19, siliquose; 20, siliquose with fallen nucleus; 21, siliquose with graviated débris; 22, purse-like, fetid. (Modified from Dor and Beard.)

some instances, however, the mass of the cataract is of a uniform white color throughout, and close inspection indicates movement within it; in which case we have to deal with a *liquid* cataract. As a rule, the consistency of a cataractous lens closely corresponds to the age of the patient.

Treatment.—Discission in any of its simple forms is the safest—if the most lengthy—procedure for the treatment of all forms of juvenile cataract before, say, the age of ten. There is an especial reason for awaiting patiently the slow process of absorption following one or more simple discissions of the juvenile cataract, instead of resorting to some of the more rapid methods, like aspiration, expulsion of the masses through a corneal opening, etc., and that is the preservation of a central, movable pupil. Although a number of operators habitually perform and recommend more expeditious procedures, yet in the latter instances the danger of an irregular pupil and hernia of the iris (with other possible complications) do not seem to compensate the shorter period of waiting and the lessened professional care. Even if by the performance of an iridectomy the therapeutic care is diminished, still the patient goes through life with a mutilated iris and an abnormal pupil.

Various *suction devices* for the aspiration of soft cataract are described.

Walker's lens-knife is so fashioned as to permit the escape of soft matter through the corneal opening made by it with a minimum danger of iris prolapse. The legends below other instruments sufficiently indicate the purpose and method of employment.

The element of time necessary to bring about discissional absorption of the lens may be ignored for infants and very young children in view of the lessened danger of the method.

When the patient is older, say from 10 years onward, discission alone or combined with suction or the removal of the discission masses through a corneal opening may be done. If the nuclear elements be sclerotic the masses remaining after the expression of the softer parts will not be readily absorbed and will be likely to cause intraocular complications. It is a question whether it is not wise (mainly to prevent incarceration of the iris) to do a preparatory iridectomy in all cases of soft cataract above the age of 10 when an opening is made in the cornea or sclero-cornea for the expulsion of cataractous masses, and particularly if one deals with a hard nucleus.

A brief reference will now be made to the principal varieties of cataract affecting the youthful lens.

Lamellar Cataract. Zonular Cataract. Perinuclear Cataract. Laminar Cataract.—This is one of the commonest of the *congenital forms* of the disease. Deutchmann first found the nucleus of the lens and the cortex to be normal but separated by a zone of degenerated fibers, interspersed with many vacuoles and minute drops of myelin. Fissures between the fibers were also present, filled with granular debris.

It is not easy to account for the pathological changes in lamellar cataract. Horner believed that a layer of pathological lens fibers was, either before or immediately after birth, deposited around a normal nucleus. He also thought that this pathological condition was due to rickets or to some similar general condition. Other observers taught that alterations in the general nutrition affect the whole lens, which at the time of development represents the nucleus. Subsequent to this formation there was a general contraction of the affected part which caused the formation of vacuoles.

Two theories of the causation of lamellar cataract are still held, one that it is due to a developmental defect, the other that it is the result of defective nutrition during the first few years of life. The main difficulty about the latter theory is that the diameter of the lens at birth is considerably greater than that of the perinuclear zone in which the bulk of the opacities in lamellar cataract are usually found. Hence, if the opacities are due to any post-natal cause it must be one that can injure not only fibers in course of formation, but fibers which are already formed, or else such a cause as would involve a great shrinking of the lens nucleus. Is it not possible that some cases may have an intra-uterine and others a post-natal origin?

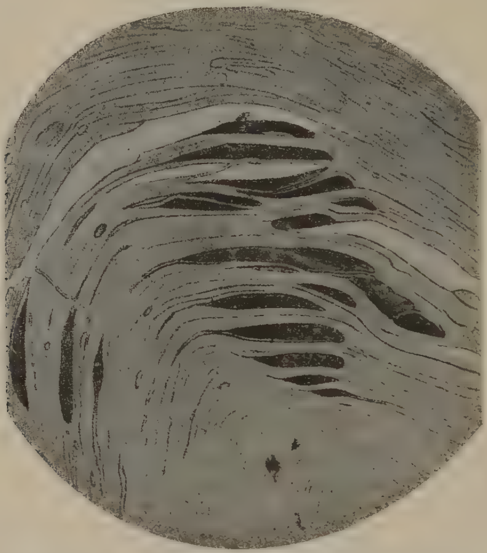

FIG. 115.—Reiterchen, *i.e.*, "riders" or "little horsemen," characteristic of amellar cataract. They are so-called because the degenerated crystalline fibres seem to ride upon the normal fibrillæ. (Hess.)

Congenital displacement (subluxation) of the crystalline lens, or **ectopia lentis,** is comparatively rare. The condition is usually bilateral and is found also as a family and hereditary trouble. Martin recorded its occurrence in five successive generations comprising 10 individuals. Before and since then numerous observers have noted the pronounced familial character and hereditary tendency.

The direction in which dislocation occurs varies and is usually symmetrical in the two eyes. In the great majority it is upwards, inclined slightly outwards or inwards, usually the former. Other positions assumed are down and in, outwards, down and out, the frequency being in the order named. As exceptions to the general rule, one lens may be dislocated in one direction and its fellow in another (asymmetrical). For instance, in two recorded cases the right lens was down and out, the left down and in; in another case the right down and in, the left up and in. Displacement backwards sometimes occurs in microphthalmic eyes as a result of some defect in

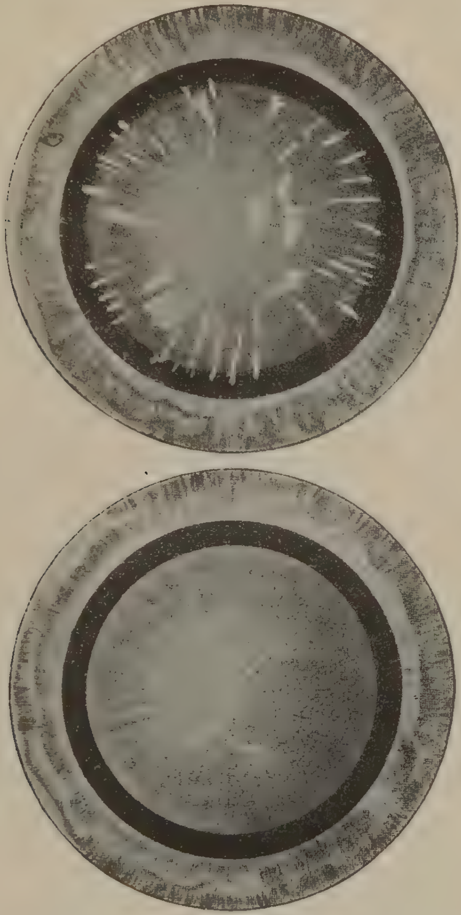

Fig. 116.—Congenital, zonular or lamellar cataracts. Above, showing "riders;" below, stellate figure at the anterior pole. (American Encyclopedia of Ophthalmology, Vol. iii.)

the development of the vitreous. Monocular diplopia is not often complained of for the reason that the pupils are usually quite small and the iris consequently hides the periphery of the lens. Knapp, however, met with an instance in which four images were perceived simultaneously with the two eyes. As seen clinically, the edge of the lens may or may not occupy the pupillary region, dilatation being necessary to see the edge, our attention being drawn to the eye primarily because of the iridodonesis. Where the pupil is large enough to reveal the lens edge, it is divided consequently into aphakic and an aphakic part, in which cases monocular diplopia must supervene. The anterior chamber is deepest on the aphakic side, the side from which the lens is displaced. The iris is found tremulous (iridodonesis). The edge of the lens by reflected light appears as a dark crescent, the lens itself being gray and the aphakic part at its margin black. The dark crescent is due to the strong prismatic refraction. The curved edge of the lens, as seen with the ophthalmoscope, is not always regular but may show slight depressions or elevations. The depression in the border may amount to a notch, constituting a coloboma. Occasionally the margin instead of being convex is nearly a straight line. The suspensory ligament as a rule is completely absent in the region corresponding to the aphakic area, the lens being dislocated away from the point of the absent zonule. Absence of the suspensory ligament produces a movable lens. Associated with ectopia lentis there are frequently found other defects, chief among which is coloboma of the iris, generally in the opposite direction, other defects being corectopia, aniridia and nystagmus.

DISEASES OF THE RETINA

This important structure forms the "sensitive plate" of the human visual apparatus, and lies between the choroid and the vitreous. Its attachment to the choroid in general is very delicate; at the entrance of the optic nerve and at the *ora serrata*, however, the union is quite firm. It may be divided into two sections, *viz.:* A large posterior section called the *pars optica retinæ*, containing the expansion of the optic nerve fibers, and extending forward to the ora serrata where it ends abruptly; and a small anterior portion, the *pars ciliaris retinæ*, which is continued forward from the ora serrata over the ciliary processes. This latter section is made up almost entirely of the pigment layer of the retina (*stratum pigmenti*).

The *ora serrata*, which reaches farther forward on the nasal than on the temporal side, marks the anterior limit of the light and form perceiving elements. The pars optica retinæ is shorter on the nasal than on the temporal side, owing to the position of the optic nerve. At the nerve head it measures 0.56 mm. in thickness; at the equator about 0.18 mm.; while at the ora serrata it thins out to about 0.1 mm.

The retina is a delicate, complex, inelastic membrane, semitransparent during life, but becoming clouded and opaque immediately after death. It is made up of a large number of layers, nine in all.

The blood supply of this membrane is derived almost entirely from the central retinal artery, which, with the accompanying vein, runs in the inner layers; the outer layers, next the choroid, are nourished by the chorio-capillary plexus. In the macular region no vessels are to be seen with the ophthalmoscope. The retinal circulation is a terminal one; there are no anastomoses with collateral branches (except with the ciliary vessels at the papilla), so that when thrombosis or embolism occurs, the area supplied by the occluded artery remains blind.

Although the infantile retina is by no means immune to most of the affections commonly found in adult life yet there are few retinal diseases confined to infancy and childhood, unless one includes certain (usually rare) *congenital anomalies* of structure, most of which are of interest only to the advanced ophthalmologist. The student who wishes to study these is referred to the larger ophthalmic textbooks and especially to the section on Congenital Anomalies of the Eye, p. 2921, IV, of the "American Encyclopedia of Ophthalmology," where they are extensively depicted and discussed.

Retinal Cyanosis.—Cyanosis of the eye is a term generally applied to both the external and internal appearances of the eye-ball in patients with general cyanosis from congenital disease of the heart. However, a cyanotic condition may be due to other causes, such as botulism, quinine poisoning, cholera, etc. Whatever the cause of the cyanosis the fundal vessels, especially the veins, are dilated and tortuous. The blood in them is darker than normal, so that the arteries resemble ordinary retinal veins. Large macular hemorrhages may be present; similar bleedings are observed near the disc and at the periphery. Vision is often normal, although it is generally much affected. In cyanotic polycythemia the retinal veins are much distended and filled with very dark blood, while the arteries are not much influenced by the disease. The ophthalmoscopic appearances in this condition were first described by H. Knapp. These cases while not very common are still not rare and many of them have been pictured and described.

In simple cyanosis retinæ, which is compatible with normal visual function, there is observed, ophthalmoscopically, besides the brown coloration of the vessels, a distention of both the veins and the arteries. The explanation of this phenomenon is that in mild general cyanosis the blood does not contain sufficient carbonic acid gas strongly to stimulate the vasomotor constriction center, and this leads through moderate stimulation to constriction of the visceral vessels, thereby forcing the blood into other organs, among them the retina, causing dilatation of its vessels.

In severe cases of general cyanosis the ocular fundus picture completely changes. The blood, overcharged with CO_2, produces marked stimulation of the medullary centers and more general vasomotor constriction, including the retinal arteries. In the ophthalmoscopic examination one sees, in fact, the veins greatly distended, and the arteries, on the contrary, unusually constricted, indeed in some places they have apparently disappeared. The constriction of the arteries leads to an intense venous stasis, and upon this follows diffuse apoplexies, venous and arterial thromboses, and also diffuse intra-ocular hemorrhages, which finally call attention to the eye-grounds. The visual function is, in these cases, rapidly and completely destroyed from the beginning of the attack.

The iris is, because of the arterial spasm, the seat of a decided venous stasis and, because it is changed into an actual blood-sponge, alters its color, so that if it were originally blue it becomes a chestnut-brown.

The iridocorneal angle is the seat of a slow inflammatory process which leads to its obliteration and to a glaucomatous condition, which may reach such a high grade that it causes rupture and subsequent atrophy of the globe. This union of intense and incurable changes of the entire eye produces a clinical picture which may well be termed cyanosis oculi, the one cause of which is an intense arterial spasm excited by carbonic acid stimulation of the medullary center. Such vessel changes have the heretofore unknown characteristic that they produce a constriction and also obliteration of the lumen of the vessels, not through the usual process of endarteritis, but by a primary contraction of the muscle coat, which later, as the result of a hypertrophy of its elements, is compensated for. A proliferation of the intima can be observed in the final stadium of the disease after thromboses and hemorrhages have occurred.

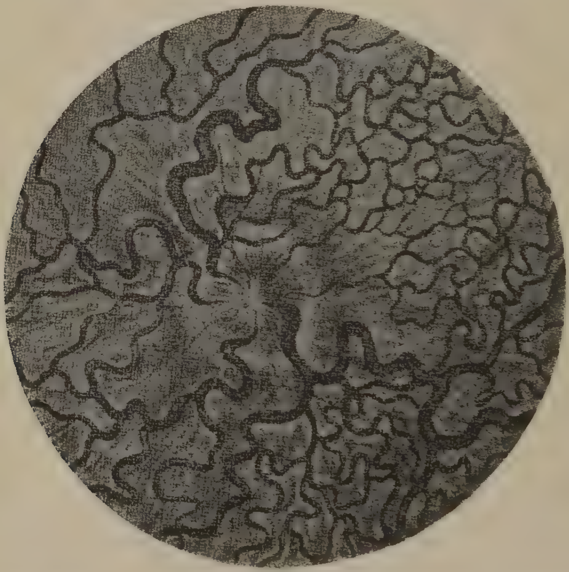

Fig. 117.—Eye ground in Baquis' case of retinal cyanosis. (American Encyclopedia of Ophthalmology, Vol. v.)

Retinitis Pigmentosa. Pigmentary Degeneration of the Retina.—This peculiar disease is not, strictly speaking, a "retinitis" but a degeneration of the optic tissues with atrophy of the retinal vessels and the accumulation and deposit of characteristic pigment in the substance of the retina. The disease is found in from 5 to 10 per cent. of deaf-mutes. It is sometimes attributed to consanguinity in the parents. The influence of consanguinity has been over-estimated. Macnamara has shown that the disease is not infrequent among the Hindoos, whose religion prohibits intermarriage. It is also hereditary. It is not infrequent in idiots, in epileptics, in the victims of hereditary syphilis, and in families subject to nervous diseases. In many cases, however, the cause cannot be determined. *The disease is either congenital or begins early in childhood*, although the pigmentation is probably never present at birth. Retinitis pigmentosa is said by Leber to be more frequent in males than in females in the proportion of about 7:3. Other congenital anomalies are not infrequently present in cases of pigmented retina.

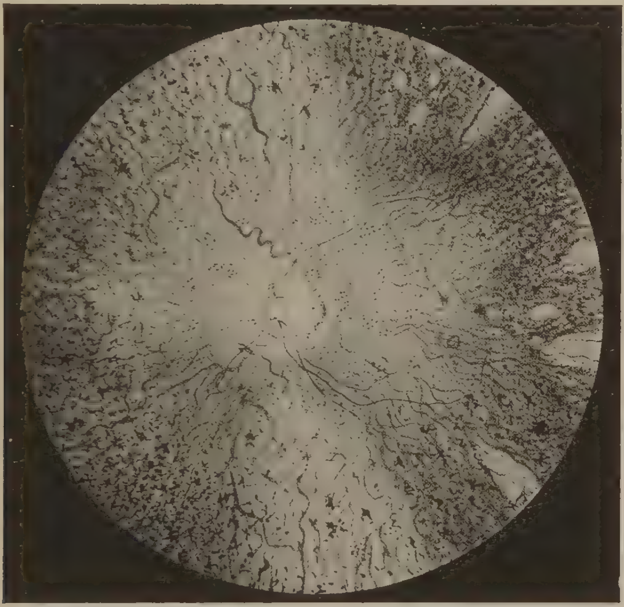

Fig. 118.—Pigmentary degeneration of the retina. (de Schweinitz.)

The **subjective signs of this disease** are (1) night-blindness, (2) loss of visual acuity, and (3) contraction of the field of vision. The most noticeable subjective symptom is night-blindness; i.e., visual acuity is disproportionately lowered under reduced illumination. Often a patient who is unconscious of visual defect by daylight must be led about at dusk or on entering a dimly-lighted room. Night-blindness may be absent, and in rare cases, with retinal hyperesthesia, vision will be best in reduced illumination. Central vision may remain practically normal for a long time, yet perimetric examination will show there is reduction of the field. A ring scotoma, partial or complete, has been observed. Usually there is reduction in central vision in proportion to the contraction of the field. In exceptional instances good central vision is retained in the presence of great narrowing of the field. This contraction leads to loss of orientation. The patient sees as if through a tube; hence the expression "tubular" or "telescopic" vision. The constant bowing of the head is characteristic. Occasionally color-blindness exists.

The *opthalmoscopic signs of pigmentary degeneration* of the retina are characteristic and include changes in the vessels, in the optic disc, and in the retina. The vessels are contracted and their number is diminished. Their walls are thickened, producing a corresponding reduction in their lumen. Often they are so small as to resemble mere threads. The optic papilla is of a creamy-white color, usully not the dead-white of atrophy. The edges of the nerve are generally ill-defined and bordered with pigment, but the presence of pigment-spots on the nerve-head is very uncommon. The lamina cribrosa is usually hidden from view, and the whole disc looks waxy or transparent. The most striking of the ophthalmoscopic appearances is the presence of irregular pigment-spots, which are most numerous at the periphery and resemble bone-corpuscles in shape. They are usually more abundant on the temporal than on the nasal side of the fundus. Often the pigmentation is most abundant along the course of the larger vessels. Early in the disease the pigment-spots are situated in the far periphery, but as time passes they encroach upon the posterior pole. As the process extends the retinal pigment layer becomes decolorized, thus permitting a view of the choroidal vessels and giving the fundus a peculiar "wainscoted" appearance. Pari passu with the growth of the stellate pigment-spot atrophy of the retina and disc become manifest. Vitreous opacities are uncommon in this disease. Posterior polar cataract is occasionally seen, but less frequently than in choroiditis.

In typical cases **diagnosis** is not difficult. The pigment-spots generally resemble bone-corpuscles, but may be rounded or irregular like the pigment collections found in choroiditis. That the pigment is in the retina is determined by the fact that the spots cover the retinal vessels. In the pigment accumulations of choroiditis the retinal vessels can be seen crossing the spots. Atypical cases of retinal disease have been described which present all of the subjective and objective signs of retinitis pigmentosa except that the pigment-spots are absent. A few cases of unilateral retinitis pigmentosa have been described. Exceptionally the pigment-spots involve the macula, while none are found in the periphery of the fundus. A few cases have been recorded of glaucoma in eyes with retinitis pigmentosa.

Night-blindness, the earliest symptom, is due to the failure of vision commencing in the part of the retina which, in the dark-adapted eye, is the most sensitive to light, that is, 10° to 20° from the fovea.

Typical cases of retinitis pigmentosa occur in which the macula alone is involved. There being no blood-vessels, at the macula, there are, in these cases, no branching pigment patches, only scattered dots and granules of pigment. The deafness and affections of the nervous system met with in association with retinitis pigmentosa are also due to abiotrophy.

The **prognosis** cf this form of retinal disease is unfavorable; most of the cases end in blindness by the time middle life is reached. While total blindness is not the rule, vision is so much reduced that the patient needs assistance in getting about. Often, however, the disease remains stationary for long periods.

Treatment.—There is no cure for this disease. The best results of treatment are obtained in the form which is caused by acquired syphilis. In all cases of retinitis pigmentosa the eyes should be used in moderation and should be protected from excessive light. Errors of refraction should be carefully corrected. The frequent use of weak miotics, the internal or hypodermic administration of strychnia, and the employment of mercuric bichlorid are among the proposed remedies. Electricity in the form of the galvanic current applied to the eye-ball has seemingly produced good results in some cases.

Retinal Disease with Massive Exudates. Retinitis Exudativa. This not uncommon but in some respects mysterious affection deserves a place in this chapter because of its frequent occurrence in childhood and its rare appearance in adults. The cases are said by Coats* to form a fairly well-defined group. They are characterized by the presence in some part of the fundus of an extensive mass of exudation. In some instances peculiar forms of vascular disease are also found. Inasmuch as the most careful physical examination commonly fails to discover any probable etiology, no certain diagnosis can usually be arrived at from the clinical standpoint. The records of pathologic examinations in such cases are extremely scanty.

The large masses are of white or yellow exudation; usually there are also groups of cholesterin crystals and hemorrhage. The affection occurs in young people, most commonly of the male sex, whose general health is usually perfect. No definite connection with former illness can be established; nor does the family history as a rule reveal anything of importance. The commencement is commonly unnoticed, and the course very slow; in some instances the eye-sight is lost from detachment of the retina, secondary cataract, iritis, or secondary glaucoma; in other instances quiescence is attained before these results ensue.

In an allied form of the disease, or in a variety of the same form, strange types of vascular disease are found—fusiform and globular expansions, kinks, loops, glomeruli, etc., as well as the more common types, such as constriction, white ensheathing, etc. The other characters of this group are similar to those of the first, but probably, in consequence of the vascular disease, the cases are less often quiescent, and are more frequently followed by the injurious sequelæ just mentioned.

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* Royal London Oph. Hosp. Reports, xvii, part 3, p. 440.

The exact significance of the vascular changes in some cases is not yet fully made out. They occur in three chief forms: Dilatation with little change in the wall; thickening of the wall with hyaline degeneration and nuclear fragmentation; collections of inflammatory cells in the wall and in the perivascular lymph spaces. Some, perhaps all, of these changes are probably secondary to obstruction caused by cicatricial contraction, and to the action of low grade irritants, such as are always produced by disintegrating blood, constituting the stimulus to the surrounding tissues, which result in the chronic inflammatory process known as organization. On the other hand, it is possible that some of the vascular changes are primary and the cause of the hemorrhage; but against this explanation are to be set the youth of the patients, and the fact that the disease is commonly unilateral. Other possible explanations of the hemorrhage are: Hemorrhage at the time of birth, hemorrhage due to constitutional conditions, perhaps associated with alterations in the coagulability of the blood, and perhaps, in exceptional cases, hemorrhage due to strain and injury. It is probable that no single hypothesis will cover all the cases.

Glioma of the Retina.—This new growth of the retina—the "amaurotic cat's eye" of the old writers—is fortunately a relatively rare disease, yet one case will be found to furnish harrowing details sufficient to impress itself permanently on the memory.

A good description of retinal glioma is given by Moores Ball.*

Wintersteiner, after an exhaustive microscopic study of these tumors, concluded that they arise from the neuro-epithelial layer of the retina, and should be named *neuro-epitheliomata.* According to their location and the direction of growth, the following varieties are distinguished. They exist only in the early stages: (1) Several nodes the size of a pinhead appear in the retina; they grow only slightly toward the vitreous, but spread in the sub-retinal space. By confluence they form a tuberous deposit on the outer surface of the detached retina: *Neuro-epithelioma exophytum* or *tuberosum.* (2) The detached retina is thickened in its entire extent or in spots; the deposits remain comparatively thin and level; later by proliferation the surface becomes uneven and protuberant: *Neuro-epithelioma diffusum* or *planum.* (3) The new growth increases only in the direction of the vitreous; the retina remains attached to the choroid; the mass spreads upon the inner surface of the retina, to which it is united not closely, but by processes; the vitreous surface of the growth is finely lobulated, cauliflower-like, or nodular: *Neuro-epithelioma endophytum.*

Unlike intra-ocular sarcoma, neuro-epithelioma is never pigmented. The tumor grows from the two granular layers of the retina, but chiefly from the inner one.

The **cause of neuro-epithelioma** of the retina is unknown. It is a disease of childhood, no true case having been found after the sixteenth year. Cases heretofore reported of greater age have been found to be either sarcoma of the choroid or pseudoneuro-epithelioma. Of 467 true cases, 314 occurred during the first three years, 62 in the fourth, and 29 in the fifth year. The disease surely is congenital in 10 per cent. of the cases, and possibly in the majority. Sex is without influence in this disease. In 25 per cent. of the cases both eyes are affected. The second eye becomes involved independently, there being no extension of the disease via the chiasma. The disease often appears in several children of the same family.

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*Am. Encyclopedia of Ophthal., vii, p. 5582.

Usually the **first symptom** is a peculiar reflex from the interior of the eye, which, from its resemblance to a cat's eye shining in the dark, was named by Beer and the older authors "amaurotic cat's eye." The parents may note that the child does not see with the affected eye. In this, the first stage, there is no pain or redness, the media are clear, the pupil is somewhat dilated, and the child's health is unaffected. Ophthalmoscopic examination shows a whitish, yellowish, or reddish-yellow mass in the fundus. The growth is covered with a plexiform network of vessels and has a smooth or nodulated surface. In this stage the growth increases slowly, and months may pass before the mass fills the globe, thus completing the second stage.

In the third stage there is increased tension. The child becomes fretful, emaciated, and cachectic. The neoplasm enmeshes all the tissues of the globe, and finally breaks out at the corneoscleral junction in front or at the optic-nerve entrance behind. Once out of the globe it grows rapidly, forming a large, ulcerated mass, which bleeds at the slightest touch. This condition was named by the older authors "fungus hematodes oculi." The organs are now involved by contiguity or by metastasis. The optic nerve furnishes a road by which the growth rapidly travels brainward. Metastases may take place in the brain, cranial bones, lymphatic glands, parotid gland, spinal cord, liver, lungs, ovaries, kidneys, submaxillary gland, or spleen. The patient dies of exhaustion.

If in a young subject the ophthalmoscope shows a whitish tumor, with retinal vessels coursing over it, and the tension is increased, the case probably is one of neuro-epithelioma. An **error in diagnosis** is possible in two directions: A tumor may be present and be overlooked, or a diagnosis of neuro-epithelioma may be made, the eye-ball may be removed, and the microscopic examination show incorrectness of the diagnosis. Hirschberg's dictum that a diagnosis between true and false retinal tumors is always possible has been found erroneous. The most careful diagnosticians have often been in error. Of 24 eyes removed at Moorfields Hospital between 1888 and 1893 for "glioma," seven were "pseudo" growths. Retinal detachment and suppurative processes in the vitreous humor cause frequent mistakes. The history of the case is always important. The parents should be questioned as to trauma, meningitis, typhoid fever, influenza, and other infectious diseases, since these may be followed by disease of the vitreous humor. If the tension is greatly increased, the case is probably one of neuro-epithelioma; if the tension is decidedly reduced, it is not neuro-epithelioma. Between these extremes are cases in which tension is normal or changes from time to time. The presence or absence of blood-vessels on the growth is important; if present, the case is probably neuro-epithelioma; if absent, the tumor is usually due to an exudative retinitis or choroiditis. Unfortunately, however, there are neuro-epitheliomata which are not vascular; and, on the other hand, exudation into the vitreous humor sometimes becomes vascularized. The "amaurotic eye" reflex is valueless in differential diagnosis. The conditions often mistaken for neuro-epithelioma, according to Wintersteiner, are: (1) Simple detachment of the retina. This is comparatively rare in childhood. Although a tumor shows a more yellowish or reddish color than a detachment, which is of a bluish tint as a rule, yet it must be remembered that, with a small tumor and a large detachment of the retina, the folds of the latter can completely conceal a neoplasm; and although the newly formed vessels of a tumor generally present a course and ramifications different from those of the retinal vessels, yet, on the other hand, there are cases which show almost no vessels. Although, as a rule, a retina which is lifted up by serous effusion vibrates and floats when the eye is moved, while a retina detached by a tumor remains at rest, yet exceptions occur. The statement that in simple retinal detachment the tension is reduced and in intra-ocular tumor it is increased must be accepted with allowances, for in the first stage of neuro-epithelioma tension is normal, and, on the other hand, in serous detachment it is often increased. (2) Leukosarcoma of the choroid. This is a comparatively rare disease of childhood. Of 259 sarcomas of the uveal tract, Fuchs found six leukosarcomas in children under 12 years of age. In these cases the symptoms of intra-ocular tumor are added to those of retinal detachment. The diagnosis is particularly difficult if the media are opaque or if the choroidal tumor perforates the globe posteriorly without causing retinal detachment. (3) Tubercles in the choroid. Here the history of the case is important. Miliary tubercles of the choroid are usually found near the optic-nerve entrance in the macular region. They appear as whitish-yellow masses or nodules in the stroma of the choroid, varying in size from one-eighth the diameter of the optic disc to the size of the disc itself. By confluence they sometimes form large masses. A rare condition is solitary tubercle, which appears as a nodule and resembles a beginning neuro-epithelioma. Diagnosis is particularly difficult in cases where the vitreous chamber is filled with granulation tissue, and in consequence of secondary glaucoma scleral ectasia appears. (4) Chronic inflammatory processes in the choroid and ciliary body. These are the conditions most often causing error. They show retinal detachment and the presence of a fibrinous vitreous exudate, which later becomes organized. The chief points in differential diagnosis are these: (*a*) In exudative choroiditis the color of the vitreous mass is a metallic, brass-like yellow, while in the retinal neoplasm whitish, yellowish, reddish, and green tints are seen; yet even here the metallic luster may be observed. (*b*) Many observers state that the exudate is non-vascular, while a retinal tumor possesses vessels. Others equally competent report cases of true neoplasm in which vessels were never visible to ophthalmoscopic examination; and, on the other hand, an exudate into the vitreous often undergoes organization. (*c*) The surface of a tumor is knobbed; that of an exudate is smooth or ragged. A tumor growing into the vitreous may have a smooth surface if it presses against the lens, while an exudate may become shrunken and conglobate. In such cases it may be impossible to make a diagnosis microscopically even after enucleation. A tumor with a smooth surface may be a neuro-epithelioma growing chiefly into the retina. (*d*) Early in neuro-epithelioma of the retina the tension is normal; later it is increased. In vitreous exudation it is usually though not always diminished. (*e*) Posterior synechiæ and other evidences of iridal inflammation are not reliable, since they may be present or absent in each condition. (5) Acute suppurative hyalitis producing a yellow mass behind the lens, inflammatory symptoms, and increased tension can be mistaken for a neoplasm. The rapid course of the disease, the presence of hypopyon, scleral perforation, and the discharge of pus will serve to clear the diagnosis. (6) Cysticercus in the vitreous can scarcely be a cause of mistaken diagnosis in this country, since it is an extremely rare disease in America, rather common in Germany. It appears as a bluish-white mass in the vitreous, without vessels, with normal tension and blindness. (7) Congenital abnormalities. In some instances eyes have been enucleated for neoplasm and examination showed persistent vascularity of the lens-capsule, and a hyaloid artery with posterior polar cataract. (8) Retinitis circinata, when occurring in children, may be mistaken for neuro-epithelioma of the retina. (9) Detachment of the retina with dropsical degeneration of the visual cells (rods and cones), according to de Schweinitz and Shumway, may exactly resemble neuro-epithelioma.

This is always a serious disease, but the *prognosis* depends upon the stage of the condition. Without treatment neuro-epithelioma of the retina always causes death. Early operations are followed by 13 per cent. of recoveries. If the growth has penetrated the eye-ball, and particularly if perforation occurs posteriorly, death is almost sure; but operation will probably prolong life. Operation for recurrence is useless. It is said that if the disease does not return within four years the patient will be exempt.

The **treatment of neuro-epithelioma retinæ** should be early and heroic. Any suspicious growth within the eye of a child calls for immediate enucleation and removal of the orbital part of the optic nerve as far back as possible. The eye should then be submitted to a competent pathologist for microscopic diagnosis. If found to be true neuro-epithelioma retinæ, the orbital contents should also be removed. This leaves a great deformity, but increases the chance of saving life. Post-operative applications of the *x*-rays should continued for several months. In cases where the neoplasm has already pierced the globe exenteration of the orbit should be done immediately, unless the disease has progressed so far that the patient cannot recover from the depression of the anesthetic and operation. If the neoplasm has invaded the cavities adjacent to the orbit, operation is contra-indicated. In a case with involvement of both eyes the same principles of treatment should apply.

THE OPTIC NERVE AND ITS DISEASES IN CHILDHOOD

The *optic nerve* proper is divided into an orbital and an intracranial portion. The nerve pierces the eye-ball at the posterior end of the optic axis, about 3 mm. to the inner or nasal side, and about 1 mm. below the horizontal meridian. Here it forms the *nerve-head*, optic papilla, or optic entrance. It is made up of nerve bundles separated by connective tissue and lymph spaces.

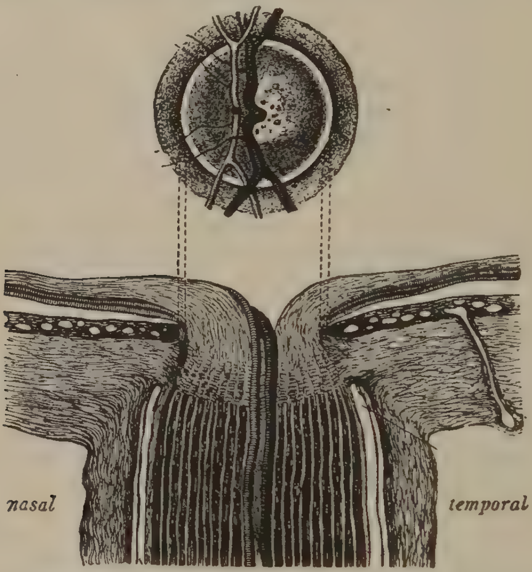

Fig. 119.—The optic nerve entrance and a sectional view as seen by the ophthalmoscope. (Fuchs.)

The *orbital portion* of the nerve extends from the optic foramen to the papilla. It is a round, S-shaped, whitish cord, 30 mm. in length, and about 5 mm. in diameter. The double curve permits of free movement of the eye-ball during its rotations.

This nerve has three sheaths, all derived from the brain coverings. The outer, or *dural sheath*, continuous with the dura mater, loosely covers the nerve and at the globe blends with the sclera. The *pial sheath*, an extension of the pia mater, directly encloses the nerve bundles as a whole, and gives off the septa that divide them from one another, thus forming part of the nervous framework. Between these two coverings is the *arachnoid sheath*, a delicate septum closely joined to the dural sheath, with which it fuses near the globe; some of the fibers are recognizable in the tissues of the sclera. The *intervaginal space* lies between the dural and pial coverings; it is incompletely divided into two subspaces by the arachnoid sheath, *viz.*, a subdura and a subarachnoid space, both of which communicate directly with the corresponding intracranial spaces. The walls of these spaces are lined with endothelium, and are probably true lymph channels. From the pial sheath and its septal prolongations into the optic nerve proper numerous capillaries are supplied to the nervous tissue, supplemented by twigs from the central retinal vessels.

In the course from the calcarine fissure in the brain the optic radiations send fibers to almost every large center—both cerebral and spinal—thus demonstrating anatomically what the ophthalmologist has long known from clinical observation, *viz.*, that almost every lesion of the brain or cord is sooner or latter followed by morbid alterations in, or functional disturbances of, some portion of the visual mechanism.

Congenital, hereditary and familial diseases and *anomalies* form the most important aspects of optic nerve pathology in children. Various tumors (*intradural* and *extradural*) are not infrequently found in childhood but they are not peculiar or confined to that period.

Hereditary optic atrophy is also known as "Leber's disease" because it was first described by him in 1871. It is an affection of the papillo-macular bundle of neurons, as evidenced by a central scotoma, and ends in optic atrophy of varying degrees. In 1877 Leber added to his previously reported cases, collecting a total of 55 in 16 families.

In 1909 E. Nettleship* collected all published and many unpublished cases of this disease; in all 180 separate records. In 150 cases atrophy appeared between 6 and 67 years, the largest number occurring at about 20 years. Nettleship characterized Leber's disease as an example of so-called "sex limited" inheritance, thus resembling color-blindness, the transmission being through apparently normal females and usually affecting only males. Consanguinity was rare; the only risk from it being when an affected male married a cousin who carried a latent liability, inherited either from her affected father or, through her mother, from an affected ancestor.

J. Taylor and G. M. Holmes† record two families showing familial optic atrophy. In the first, three out of four living male children were affected, two sisters being unaffected. The parents had good vision. Beyond them the family history was not obtained. In the second family, three out of six males had the visual defect of Leber's disease, while the four females were not involved.

Fisher suggests that the causal agent in Leber's disease might be a disturbance of the pituitary body, of temporary duration and moderate in degree, implicating the visual pathway. If such a view is correct organo-therapy might be expected to do good. As is well known, during pregnancy the pituitary gland may be enlarged to two or three times the normal, and a milky secretion can often be squeezed out of it. There is known to be a close relationship between the pituitary and sexual glands. Moreover, the pituitary and the optic chiasm are in such close contiguity that any small swelling of the former may extend to and make itself felt in the latter. If the lesion which gives rise to these symptoms is due to some disorder of the pituitary body, it also must be temporary and transient, hence in an active and recent case of Leber's disease it might be of great help to have an early Roentgen-ray examination of the sella turcica.

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† Trans. Ophthal. Soc. of Un. Kingd., xxix.

* Trans. Ophthal. Soc. of Un. Kingd., xxxiii (1913), pp. 95 and 116.

DISEASES OF THE ORBIT AND ITS CONTENTS

With the exception of **congenital tumors of the orbit** there is little to be said about the pathology of this region that does not apply equally to the adult orbit. It may, however, be noted that **orbital cellulitis** in its various forms—the most common and most important of the orbital infections—is very rare in children, because of the undeveloped conditions of the infantile accessory sinuses.

Anophthalmia, the so-called congenital absence of the eye-ball, is, generally speaking, a misnomer, as in most of the cases the globar elements can be found in the depths of the orbit. **Microphthalmos** or undeveloped eye-ball is, on the other hand, a comparatively common anomaly. The latter is often associated with cystic formations and other organic alterations.

Unless it is of the greatest urgency neither *enucleation of the globe* nor *exenteration of the orbit* should be done in children before development and growth of the face are complete. These procedures tend to produce asymmetry of the parts, in some instances amounting to a quite noticeable deformity when the young child has subsequently attained the adolescent period. Of course there may not be, as in the case of malignant neoplasms, any alternative; in which instance every means (particularly the early, careful and constant wearing of proper protheses) should be employed to encourage the development of the bony structures of face and orbit.

Of **tumors of the orbit** presenting special juvenile characters and originating during or before the period of the first dentition, the *congenital* varieties are the most numerous. Of these, **dermoid cysts** are the most common. They do not greatly differ from these growths in other parts of the body. For example: Bogatsch* from the right orbit of a youth of 17 years removed a large dermoid cyst. The eye had protruded somewhat since birth, but much more within the last eight years. Rumszewicz has reported two cases of teratoma, the growth in each instance being deep in the orbit and associated with the bony wall by connective tissue bands. Histologically the tumors were found to contain neuroglia cells, hairs, smooth muscle cells, and cartilaginous and bony tissue.

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* Ophthalmic Year-book (1912), p. 374.

Infantile Glaucoma. Ox-eye. Keratoglobus. Buphthalmos. Hydrophthalmos.—Because of its peculiarities and strongly marked differences from the adult disease a few paragraphs are given to this formidable disease. It is characterized primarily by a uniform spherical bulging of the whole cornea. It generally takes the form of infantile or congenital glaucoma. The increase of size extends to the neighboring parts of the sclera and often involves the whole eye-ball. True buphthalmia is always congenital.

As Parsons points out, the most striking feature in buphthalmia is the large size of the cornea (hence the term "magalocornea") which may be opalescent, dull, bluish, or it may even be quite transparent. The anterior chamber is very deep, the media clear. The distension of the globe is marked by more or less proptosis and by the blue color of the sclerotic, especially near the limbus, due to thinning. Sometimes there is nystagmus. The globe is much enlarged, usually oval and elongated, though the plasticity of the young tunics is shown by an unusual increase in diameter of the corneal base. The mean dismensions of 20 buphthalmic eyes gives the following results:

	Maximum	Mean	Normal
Antero-posterior...............	38.8 mm.	32 mm.	24.3 mm.
Vertical.....................	28.6 mm.	26 mm.	23.6 mm.

Of 10 cases in which careful measurements were made of the anterior chamber the maximum depth was 12.8 mm., minimum 3.0 mm., mean 6.3 mm., normal 2.6 mm.

As Abadie*properly says, congenital buphthalmos is without doubt among the most distressing of maladies; children who are attacked with it being doomed to almost certain blindness, while the deformity of their eyes is one of the saddest of objects. Iridectomy in buphthalmic glaucoma, says Abadie, furnishes more disasters than successes. Miotics, so useful in those forms of glaucoma in which iridectomy is not justifiable, do not help.

In fact, buphthalmos is essentially a condition quite different from most varieties of glaucoma. There is hypertension and a secondary excavation of the optic papilla, but there is also a chorio-retinitis which is generally overlooked because the cornea is less transparent than normal and deep exploration of the eye impossible. Later, when the fundus can be seen, there is found papillary excavation; more often no trace of the chorio-retinitis is discovered, because in the equatorial, and especially in the ciliary, region the lesion often escapes detection. If the pupil is sufficiently dilated and the patient's eye directed laterally, there may be seen atrophic, discrete spots (sometimes confluent, gray zones) bordered by pigment deposits so characteristic of the pathologic change. After a careful examination if the chorio-retinitis is not discovered it should not be concluded that it does not exist; Abadie believes in that case the disease is latent and as yet the ophthalmoscopic lesion has not appeared. Persuaded that in buphthalmos it is the chorio-retinitis which plays the fundamental rôle, Abadie directs his therapuetic measures against that disease, giving intramuscular injections, which he believes to be more efficacious than inunctions. Abadie claims that in all of his cases this treatment has produced beneficial results. One case especially, in which the right eye was the larger and on which several sclerotomies had been done with no other result than an iridic hernia, mercurial injections improved vision and the tension became normal.

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*La Clinique Ophtal. (June 10, 1907).

It is the experience of many surgeons that, on the whole, Elliot's operation (the trephine opening made well forward in the cornea if that coat be not too much thinned by the stretching characteristic of the disease), or Lagrange's procedure gives the best results when done early in the process.

ANOMALIES OF THE OCULAR MUSCLES

The one pathological condition of the eye muscles in children about which the well-grounded pediatrist should be well informed is *squint* in its various forms. Something has already been said on the subject under "*Examination of the Eyes*" in this chapter. Although the actual conduct of strabismic cases requires the services of an expert ophthalmic surgeon, yet a fairly clear conception by the pediatrist of the little patient's present condition, prospects and needs will be of exceptional value in accomplishing desirable results in a given case of strabismus.

The two commonest forms of squint will now be considered: *Convergent strabismus,* in which one eye *turns in,* and the *divergent* variety (rarer, and uncommon until puberty is reached) in which the squinting eye *turns out.*

As Moores Ball* has pointed out, deviations of the visual axis may have their origin in anomalies of refraction, structure, and insertion of the ocular muscles, and they may be influenced by the development of the orbits, by innervational disturbance, and as the result of congenital and acquired monocular amblyopia (opacities of the media and diseases of the fundus).

Comitant Convergent Squint (**Esotropia**).—There are three varieties recognized: *Permanent monocular, permanent alternating,* and *periodic.*

Permanent monocular squint is the most common. It usually makes its appearance when the child first begins to be interested in near objects, such as toys, picture-books, etc.—about two years of age. It may, at first, be periodic, but soon becomes permanent and monocular. Its origin is almost invariably attributed by the laity to whooping-cough, fright, imitation, or to the attraction of the child's sight to some object hanging overhead. The most frequent, but not the only, cause is a hypermetropic refraction. This operates to produce it through the excessive convergence of the visual axes, which accompanies the extra amount of accommodation required in hypermetropia to see distinctly at a given distance. Normally, for each degree in the angle of convergence an equal degree of accommodation is employed. In the hypermetrope this balance is disturbed from the beginning, since, in order to see distinctly at a distance, the hypermetrope must accommodate to the degree of his hypermetropia and still maintain parallelism of the visual axes. Now, when it comes to viewing an object at near range, say at 33 cm., the hypermetrope will require as many dioptres of accommodation in excess of the three dioptres normally associated with three meter angles of convergence as he has dioptres of hypermetropia, and as a result of this one of two conditions must prevail: Either he must be satisfied with blurred, but single, vision (both eyes converged to the object, but accommodation insufficient), or he may secure distinct vision (both eyes accommodated for the object, but convergence excessive), which will produce double vision unless he permits one eye to turn in, and this is the solution of the difficulty which the patient instinctively accepts. Ninety-eight per cent. of cases of convergent squint are hypermetropic.

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* "Modern Ophthalmology," pp. 675–677.

In convergent squint the result of hypermetropia, the deviating eye, in more than half the cases, is found to be amblyopic. The causal relationship between the squint and the amblyopia still remains in dispute, some authorities looking upon the ambloypia as the result of the squint from disuse of the eye, and others regarding it as the cause of the squint by removing the stimulus to convergence which would be excited if there was a tendency to diplopia. The absence of diplopia in comitant strabismus may be due to the suppression of the retinal image, or it may arise from the development of new identical points in the retina of the deviating eye.

Comitant Divergent Strabismus (**Exotropia**).—The same varieties of this form of squint may be recognized as of convergent strabismus. The permanent monocular variety is the most common, but the alternating is more frequent than in convergent squint. As a rule, divergent squint appears later in life than does convergent, because it is usually associated with high degrees of myopia, which condition, for the most part, is an acquired anomaly. This operates to produce it through the lessened amount of accommodation required to see distinctly at near distances, in consequence of which the convergence impulse is lessened, and as the near point approaches with the increase of the myopia a point is reached where the interni are no longer equal to their task and divergence results. It is also seen as a sequel to insufficiency of convergence—a condition which may be met with in any state of refraction. Excessive divergence of the axes of the orbit in the course of the development of the skull may also lead to divergent strabismus. Diplopia is of more frequent occurrence than in convergent squint, probably because binocular vision has been maintained to a later period of life.

The pedriatrist may gain a fair idea of the proper *treatment of squint* from the recent experiences of Bishop Harman* who found this condition in girls twice as frequent as in boys. Out of 1400 eye patients examined 199 were squinters—191 convergent and 8 divergent; fixed in 166, alternating in 16 of 182 uncomplicated cases. He thinks squint a reversion, a return to the monocular vision which is normal in the lower vertebrates. It is the brain which controls binocular vision, through the fusion faculty and through stereoscopic vision, which is the outcome of the variation in angle of view.

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*Am Encycl. Ophthalm., xvi, p. 12279.

Harman divides the *treatment of squint* into three stages: First, balancing the visual acuity; second, awakening the fusion faculty; third, operation. The first includes complete cycloplegia and careful refraction, with correction to be worn no matter how early in life, the carrying frames being occasionally tied on for young children. The second, training, is by covering the better eye several hours each day, or by atropin in the better eye. Stereoscopic training by the method of Darwin (first published in 1778) and by the more modern methods are also employed. The influence of any such practice is in proportion to its continuity, but it prepares the way for surgical measures.

Operation is put under four considerations: (1) The rationale of the procedure. (2) The most favorable time. (3) The best technique. (4) The prospects of success. As to rationale, operation on the case may be thought of as to the cosmetic or as to the binocular value. Conditions are favorable for operation even if the vision is reduced to 33 per cent., and the earlier it is done the better. If the child goes to 9 or 10 years of age with no improvement, operation may be done for cosmetic effect. In alternating types there is no value in training, and operation may be done early.

Harman summarizes the first 100 cases of operation as follows: Males 43; females 57; 48 were 10 years of age or under; 39 were 10 to 20 years; 12 were 20 to 30 years; 1 over 30; 93 were for convergent (57 fixed and 36 alternating); 6 divergent; 1 vertical; 81 cases had correction at the first operation; 19 cases showed partial correction.

Results were:

Binocular vision restored in (the small number being due to lateness of operation)	4	
Cosmetic correction complete in	36	
Cosmetic correction error less than 3°	22	
Cosmetic correction error above 3°	23	
Successful		85
Uncorrected 6 to 10°	9	
Uncorrected 10 to 20°	4	
Over-corrected	1	
Diseased	1	
Unsuccessful		15
		100

Organic muscular anomalies in children are not very rare; nor are certain type of congenital *oculomuscular pareses* (ophthalmoplegia), most of the latter of uncertain etiology.

Congenital ptosis (dropping of the upper lid) is the commonest. It is often associated with *epicanthus.* Hardy tells us that it is most frequently bilateral, though unilateral cases appear especially in conjunction with other muscular anomalies. It occurs about equally in both sexes. The isolated cases are frequently attributed to injury at birth. When looking straight ahead the defect may not be very noticeable. In other cases the patient assumes a characteristic appearance. The skin of the forehead is thrown into transverse folds by the action of the occipito-frontalis. It is by this means that the patient in his attempts to see lifts the eye-lid sufficiently to uncover the lower portion of the pupil. The loss of power in the levator may be complete or incomplete. In the former, the drooping is greater and in addition to the use of the frontalis the patient tilts the head backwards. Frequently there are defects in the development of the other muscles about the eyes.

With ptosis there is at times a defective development of the facial muscles with epicanthus to which the term "mask-like epicanthus" has been applied. Another interesting condition is that of *ptosis with associated movements* wherein movements of the jaw produced striking effects in the lid suffering with ptosis. Thompson and Souter have given a detailed description of a case observed by them in a girl of nine years with ptosis of the left upper lid. Upon working her jaw to the right a marked upward jerk occurred in the left upper lid exposing 2 to 3 mm. of sclera. Coburn's patient showed complete ptosis except that the upper lid could be raised by opening the mouth.

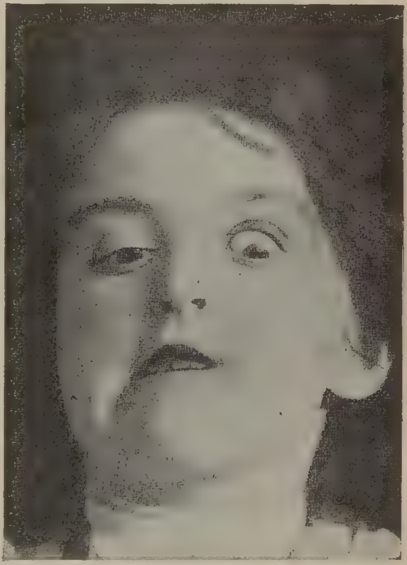

Fig. 120.—Congenital ptosis with associated lid movements of the affected eye. (Thomson and Souter.)

Injuries of Children's Eyes.—These do not greatly differ from similar accidents in adult life although the environment of infancy and childhood naturally expose the younger element to special forms of traumatism.

Birth injuries are rather important, *obstetrical damage to the cornea* in particular. De Wecker in 1896, Truc in 1898, as well as Thomson and Buchanan in 1903, reported cases in which the corneal tissues were injured by the use of the obsterical forceps. At least three different lesions of the cornea were noticed. Parsons describes these, first, as a diffuse opacity, indeterminate in position, which is permanent. It is also due to edema but probably with consecutive inflammatory changes, and rupture of Descemet's membrane. Third, an opacity, linear in form and permanent, due to a rupture of Descemet's membrane and sometimes of the posterior corneal lamellæ. Probably in some of the cases injury is due to direct pressure of the blade of the forceps on the cornea. E. v. Hippel has reported rupture of Descemet's membrane without laceration of the corneal substance. He believes that it may be due to sudden increase of intra-ocular pressure during birth. Traumatic keratitis was seen by Thomson and Buchanan in eight cases, involving 12 eyes. The opportunity of observing so many cases is owing to the prevalence of rickets (associated with contracted pelvis) in Glasgow.

Hyphæma, rupture of the choroid, retinal hemorrhages, luxation and avulsion of the globe, fractures of the orbital walls have, among other obstetrical traumas, also been reported. Some injuries may be due to the finger of the accoucheur. In many cases orbital fracture has been caused by the forceps and the mechanism of the injury seems to be in the first place the forcing forwards of the globe by the diminution of the orbital space with the forceps, and secondly the arrest of the protruded globe under the unduly exaggerated promontory of the contracted pelvis. *Avulsio bulbi* due to this cause shows the double action of pressure from behind effecting the protrusion and traction from in front tearing the eye-ball out. The muscles separate near their tendinous insertions into the globe, the external rectus most frequently escaping. The optic nerve has been ruptured a short distance behind the globe.

Rupprecht* saw a slight diffuse parenchymatous haziness of the cornea with impressions above the eye of a newborn, delivered with forceps (narrow pelvis of the mother). Apparently the right blade of the forceps had been applied to the right eye. The child died the next day. Descemet's membrane presented two dehiscences, ⅓ and ⅔ mm. wide, and there were extensive hemorrhages between choroid and sclera, and within and in front of the retina. The forceps apparently had pressed the cornea into the interior of the eye like a rubber ball, causing ruptures of the now convex inner surface of Descemet's membrane.

E. von Hippel found in the eye of a newborn child hemorrhages at the fovea and in the vitreous, which perhaps had also been produced by the forceps.

John Green, Jr., has also noted an opacity of the cornea due to injury received at birth. This, he says, may be diffuse and transitory, or of a linear or irregularly striped aspect, and permanent, depending on edema of the cornea due to tears of Descemet's membrane. He further points out that exophthalmus may be caused by compression of the skull or by a direct backward pressure of forceps, acting like the speculum which dislocates the globe in enucleation. Subconjunctival extravasations are usually accompanied by other injuries, as are hemorrhages into the anterior chamber. Optic atrophy may follow fracture running through the optic foramen. The lids may be bruised, cut, or partially torn off; even the globe may be gouged out. Traumatic cataract, oculomotor palsy, iridodialysis, rupture of the choroid, deep intra-ocular hemorrhage, have also been noted, all after the use of forceps in delivery. Not over 25 per cent. of recorded cases can be classified as severe. Minute retinal hemorrhages are rather common. Many injuries are found to have occurred in non-instrumental delivery, as after version, in face presentations, spontaneous deliveries, breech presentation, and so on. Considering that it is frequently a question of losing or saving two lives, a possible injury to the child's eyes can hardly weigh as a serious contra-indication to the use of forceps, but the grave possibilities should always be borne in mind. Any marks of violence to the eyes or ocular adnexa should lead to thorough examination.

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* Kl. Monatsbl. f. Augenheilk. (1908), p. 134.

CHAPTER CXCI

HOSPITALS FOR INFANTS AND CHILDREN

Adminstration, Organization and Management

By John M. Dodson, M.D.

Chicago, Ill.

Architecture and Construction

By Richard E. Schmidt, F.A. I. A.

Chicago, Ill.

The hospital is an essential agency in modern medicine. Many cases of illness, medical as well as surgical, can be given adequate study and care only within a well-organized, properly equipped hospital. Such diagnostic appliances as the *x*-ray, the more refined methods of chemical and bacteriologic diagnosis, and, most important of all, the service of a group of experts in the several specialties of medicine and surgery, can be secured only in such an institution. This is true for infants and children, as it is for adults.

Hospitals should be so multiplied and distributed that every sick person needing the medical service which they alone can render may find it possible to secure such care and treatment.

In this movement for the extension as well as the improvement of hospital service, the initiative must come, for the most part, from the medical profession, and to its members the community looks for advice and guidance.

History.—The history of hospitals is very ancient. There is ample evidence that such institutions, or at least what corresponded to our modern dispensaries from which hospitals were developed, existed in Egypt in the eleventh century B.C. In the fourth century B.C., King Asoka in India, commanded the establishment of hospitals throughout his dominion, and the hospitals established by this order continued in existence for at least 1100 years. In Greece and Rome, and in all later civilized nations, hospitals have been provided in greater or less numbers. These earlier hospitals were general hospitals, receiving all types of cases.

Special hospitals, devoted exclusively to the care of patients afflicted with some one disease, *e.g.*, tuberculosis, or a special group of disorders like those of the eye, the ear, nose and throat, or to diseases of a certain age period, like those of infants and children, are quite modern, dating back less than a century (if we except those for the care of the insane). Naturally such hospitals did not arise until the several specialties in medicine were recognized and well established.

In the United States, the establishment of the first hospitals devoted exclusively to sick children dates back little more than 60 years, if we exclude from consideration such institutions as Orphans' and Foundlings' Homes, Infant Asylums and the like, intended primarily for unfortunate but not sick children.

The Children's Hospital in Philadelphia was established in 1855, the New England Hospital for Women and Children, Boston, in 1863, and the New York Foundling's Hospital in 1869, St. Mary's Free Hospital for Children, N. Y., in 1870, St. Christopher's Hospital for Children, Philadelphia, in 1876. The Nursery and Child's Hospital, Baltimore, 1878. Few, if any, other hospitals for sick children were established previous to 1880.

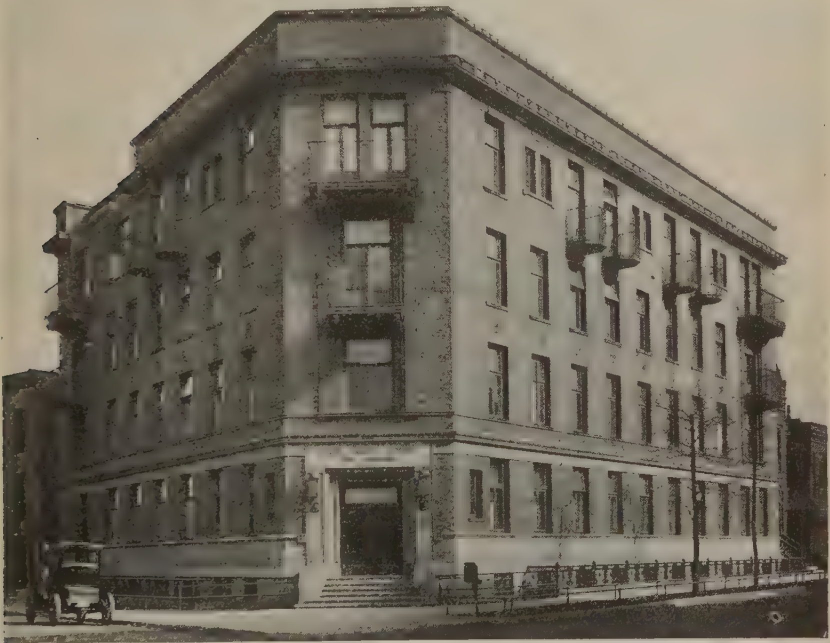


FIG. 121.—Sarah Morris hospital for children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

Prejudice against Hospitals.—Notwithstanding the long period during which hospitals have been recognized as suitable places for the care of the sick, an intense prejudice against them, amounting oftentimes to real fear, prevailed for many centuries, a prejudice which has been, to any degree, allayed only within the last 50 or 60 years. It was the inevitable accompaniment of the dreadful mortality rate in the hospitals of former times. This high mortality was due, for the most part, to the surgical and obstetric infections and the transmission of communicable diseases, the danger of which is much intensified when the sick, in large numbers, are in close proximity, and are being cared for by the same nurses, attendants and physicians.

It is little wonder that women shuddered at the thought of entering a hospital for confinement, when, as happened in the obstetric wards of the best of the old-time hospitals, often 40 to 50 per cent. and sometimes as high as 70 per cent. of women delivered in these institutions died of puerperal infection, while in the surgical wards of the same institutions hospital gangrene and other surgical infections were uncontrollable. Happily the demonstration by Pasteur of the germ origin of these infections, the development of antiseptic surgery, and the discovery of effective means of controlling the spread of many communicable diseases, have entirely revolutionized hospital conditions and hospital practice. Some lying-in hospitals report as many as 1100 consecutive deliveries without a case of puerperal sepsis. The transmission of a surgical infection, from one patient to another no longer occurs in any well-conducted institution, and the conveyance of a contagious disease, such as measles, scarlet fever or diphtheria can be practically abolished by proper management.

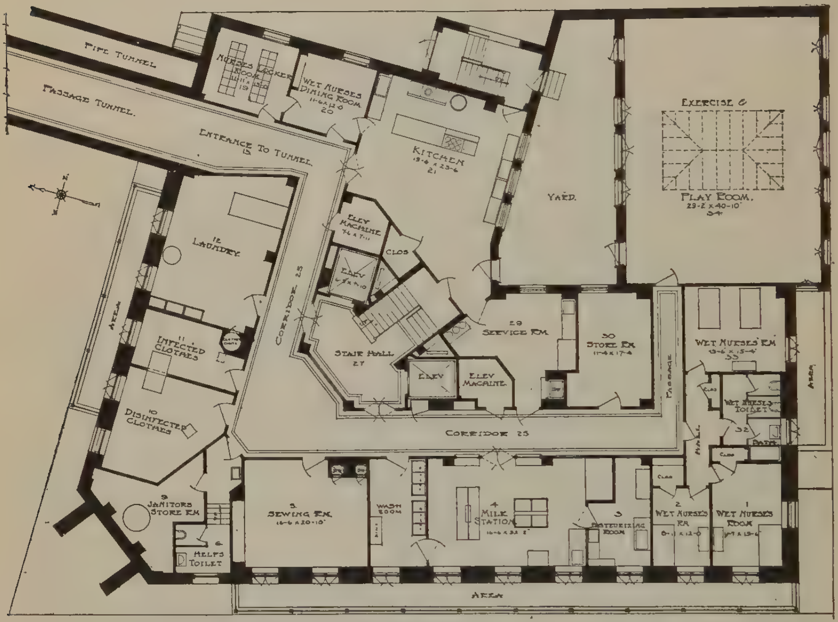


Fig. 122.—Basement, Sarah Morris Hospital for Children, Chicago, Ill. Food, heat, light and power service is obtained from Michael Reese Hospital by tunnel indicated on the plan. (Richard E. Schmidt, Garden and Martin, architects.)

In the Anna Durand Hospital of the John McCormick Memorial Institute for Infectious Diseases there have been received in the eight years since it was opened (1913–1921) 4895 patients afflicted with communicable diseases, among them scarlet fever, diphtheria, measles, mumps, whooping-cough, epidemic menigitis and epidemic poliomyelitis. In 67 of these patients two diseases were present on admission, usually scarlet fever and diphtheria. In 35 other patients a second disease developed within such a period after admission as to make certain that it was acquired before entrance to the hospital. In only 37 patients was a second infection acquired after admission to the hospital, seventy-six hundredths of 1 per cent.

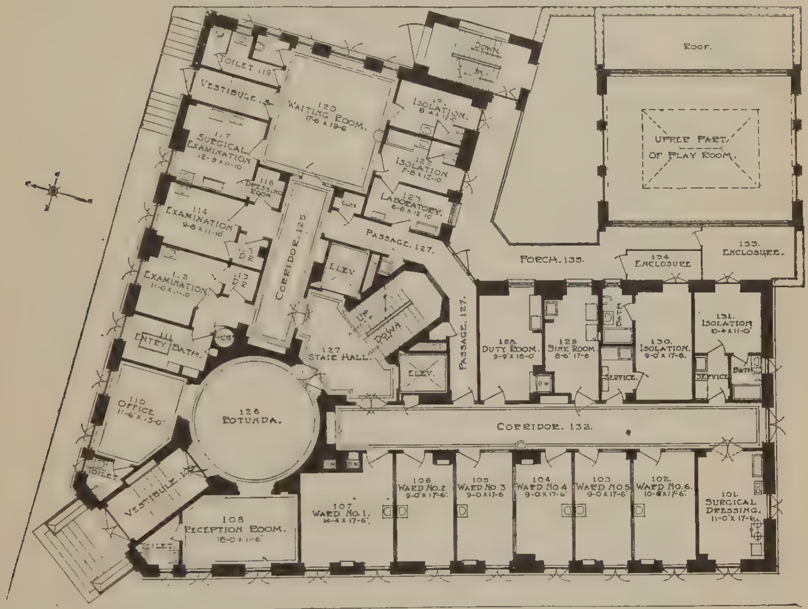


Fig. 123.—First floor, Sarah Morris Hospital for Children, Chicago, Ill. Note complete arrangement for examination of prospective patients, segregation and observation. Medical, food and other service can be given to certain rooms without entering the remainder of the building. (Richard E. Schmidt, Garden and Martin, architects.)

Such facts as these have gradually become known to the people at large, and it is becoming generally realized that a well conducted hospital is the safest, most economical and altogether the best place for the care and treatment of many patients with serious illness. This prejudice against them retains its hold more strongly in regard to infants and children than in the case of adults, but is being allayed. At the same time there is yet much to be accomplished in the conduct of hospitals for children in the matter of preventing the spread of communicable diseases. Unfortunately the happy experience of the Anna Durand Hospital has not often been duplicated.

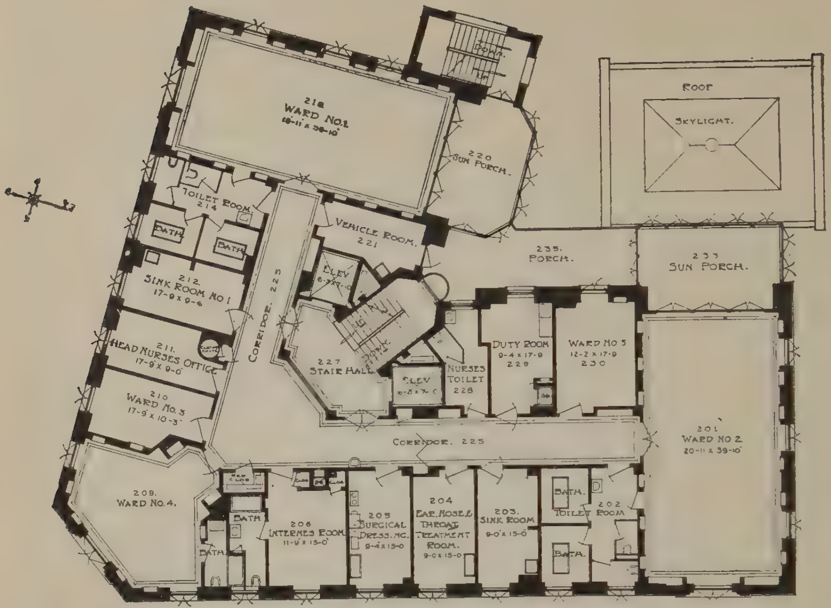

ROOF
SKYLIGHT
218 WARD No.1 18-11 x 38-10
DOWN
UP
220 SUN PORCH
TOILET ROOM 214
BATH
BATH
VEHICLE ROOM 221
235 PORCH
233 SUN PORCH
212 SINK ROOM No 1 17-9 x 9-6
CORRIDOR 225
ELEV
211 HEAD NURSES OFFICE 17-9 x 9-0
227 STAIR HALL
ELEV
NURSES TOILET 228
DUTY ROOM 9-4 x 17-9 229
WARD No 5 12-2 x 17-9 230
210 WARD No 3 17-9 x 10-3
201 WARD No 2 20-11 x 39-10
CORRIDOR 225
209 WARD No.4
BATH
BATH
206 INTERNES ROOM 11-9 x 15-0
205 SURGICAL DRESSING 9-4 x 15-0
204 EAR, NOSE & THROAT TREATMENT ROOM 9-0 x 15-0
203 SINK ROOM 9-0 x 15-0
BATH
202 TOILET ROOM
BATH

FIG. 124.—Second floor, Sarah Morris Hospital for Children, Chicago, Ill. Note the corridor doors by means of which the floor can be divided into two units. (Richard E. Schmidt, Garden and Martin, architects.)

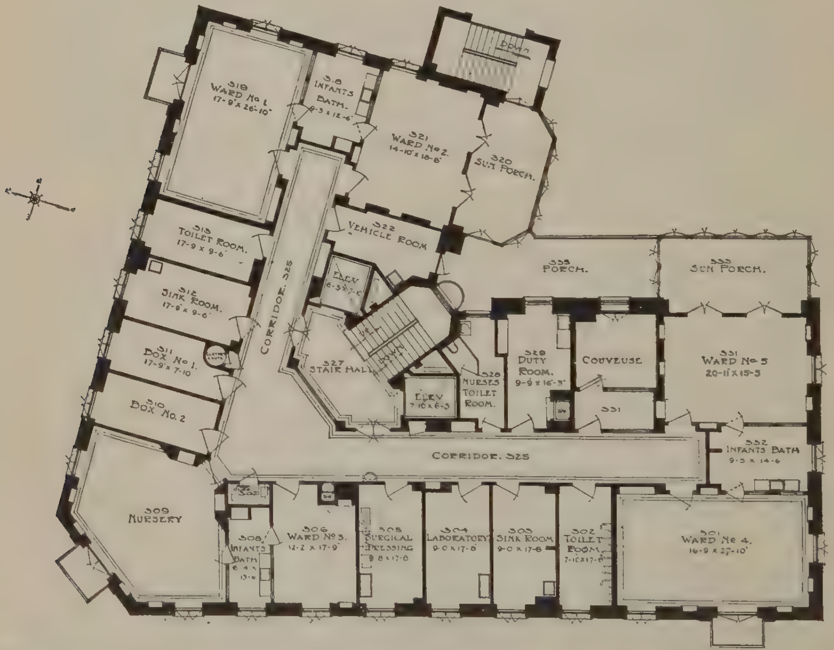

318 WARD No 1 17-9 x 26-10
319 INFANTS BATH 9-3 x 12-6
DOWN
321 WARD No 2 14-10 x 18-8
320 SUN PORCH
315 TOILET ROOM 17-9 x 9-6
322 VEHICLE ROOM
ELEV
CORRIDOR 325
333 PORCH
333 SUN PORCH
312 SINK ROOM 17-9 x 9-6
311 BOX No 1 17-9 x 7-10
327 STAIR HALL
328 NURSES TOILET ROOM
ELEV 7-10 x 6-3
329 DUTY ROOM 9-9 x 16-3
COUVEUSE
331
331 WARD No 5 20-11 x 15-5
310 BOX No 2
332 INFANTS BATH 9-3 x 14-6
CORRIDOR 325
309 NURSERY
308 INFANTS BATH 6-4 x 13-6
306 WARD No 3 12-2 x 17-9
305 SURGICAL DRESSING 9-8 x 17-8
304 LABORATORY 9-0 x 17-8
303 SINK ROOM 9-0 x 17-8
302 TOILET ROOM 7-10 x 17-8
301 WARD No 4 16-9 x 27-10

FIG. 125.—Third floor, Sarah Morris Hospital for Children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

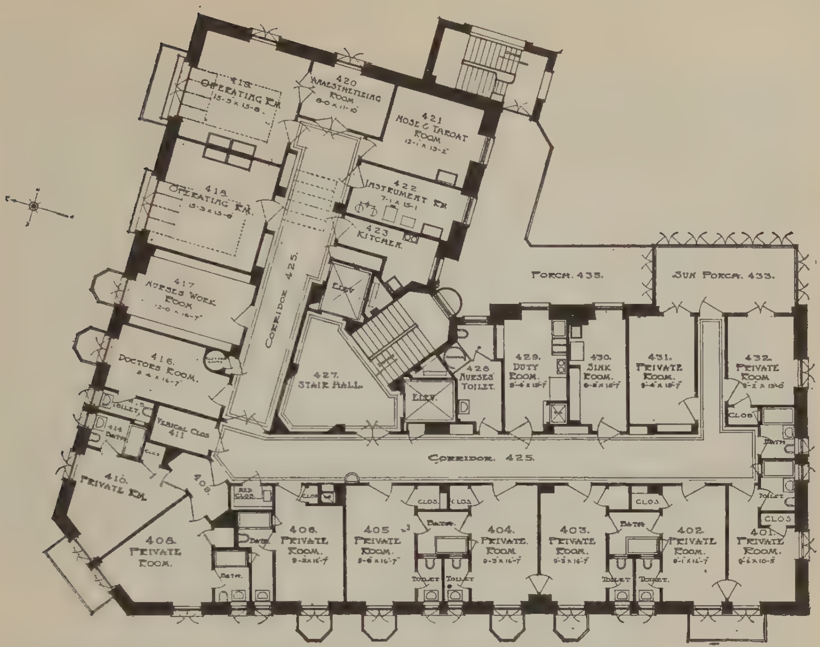


FIG. 126.—Fourth floor, Sarah Morris Hospital for Children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

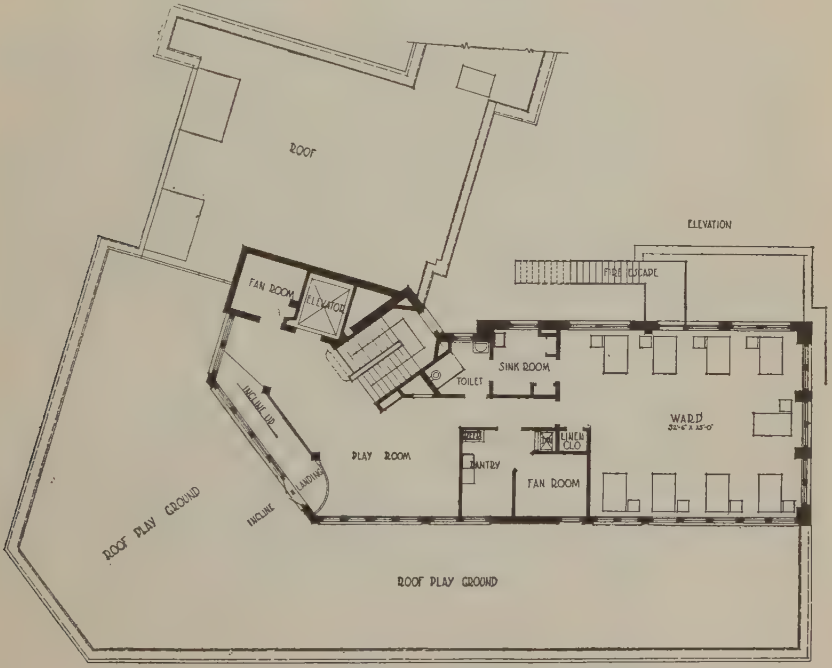


FIG. 127.—Fifth floor, Sarah Morris Hospital for Children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

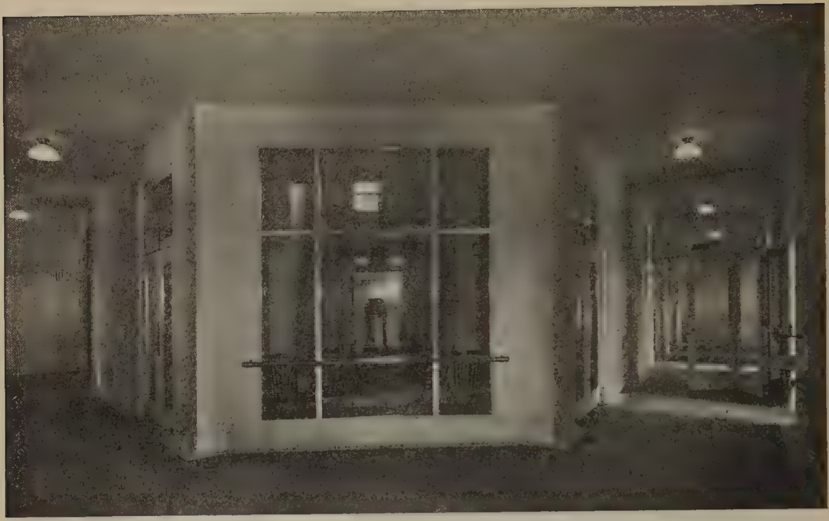


Fig. 128.—Corridors, Sarah Morris Hospital for Children. Note cross corridor partition doors and glass partition between corridor and visitors' waiting room. (Richard E. Schmidt, Garden and Martin, architects.)

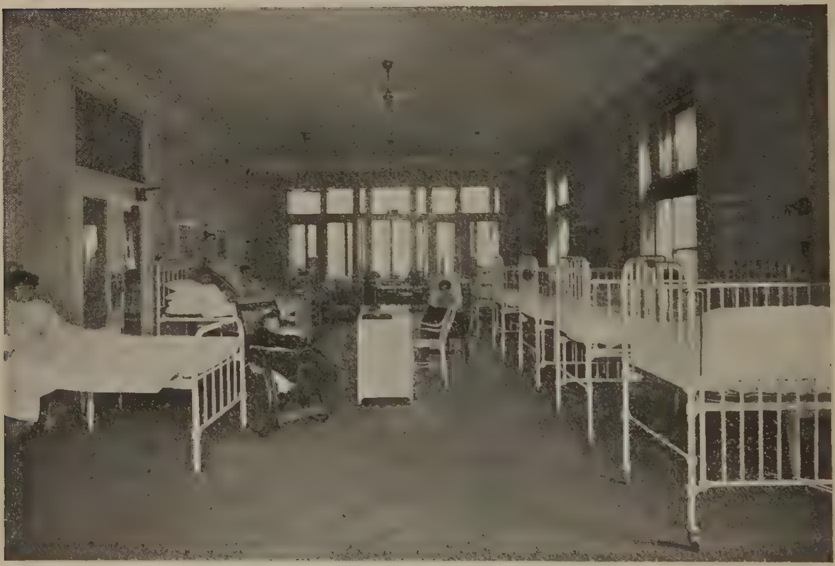


Fig. 129.—Children's ward, Sarah Morris Hospital for Children, Chicago, Ill. Individual wall cabinets, ward porch, sliding bed sides and ceiling fans. (Richard E. Schmidt, Garden and Martin, architects.)

Functions of a Children's Hospital.—The functions of a children's hospital include:

I. The care and cure of the sick, comprising:

1. The study of a difficult case for the purpose of arriving at a diagnosis.

2. The study of a patient, e.g., one of artificial feeding of an infant, in order to determine the best procedure to be followed in the home.

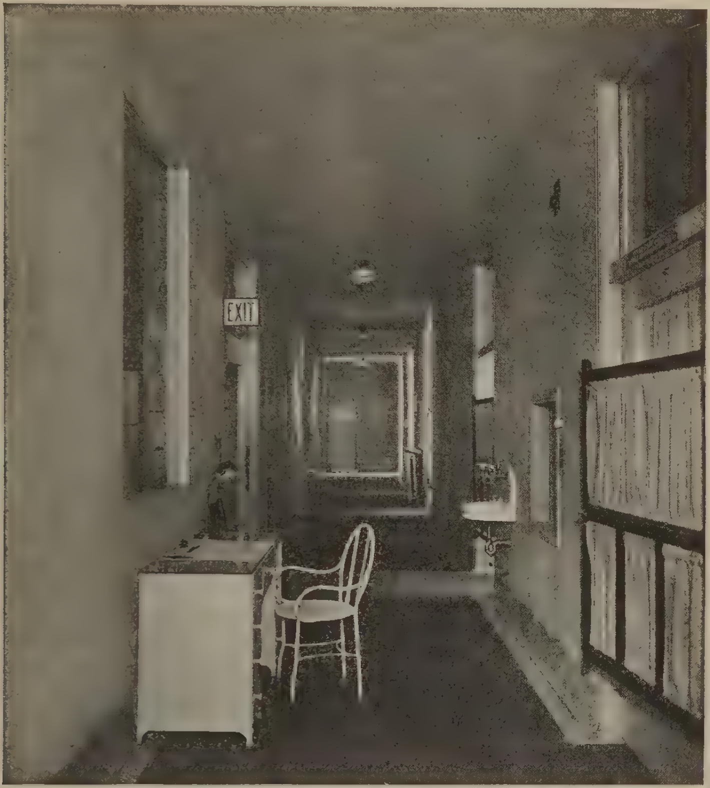


Fig. 130.—Sarah Morris Hospital for Children, Chicago, Ill. Corridor showing screened or half door to wards or private rooms. Rolled steel frames and casings, terrazzo base, plinths and borders—recessed linoleum floor covering, and refrigerated water drinking fountains. (Richard E. Schmidt, Garden and Martin, architects.)

3. The more prolonged treatment of infants and children with severe illness and of those whose home conditions do not permit of suitable care.

4. The performance of surgical operations which can be done more safely, effectively and economically than in the home.

5. The isolation and treatment of cases of communicable disease.

The thorough exhaustive study of an obscure case of disease often requires the employment of x-ray photographs—frequently a series of them—of fluoroscopy, of the more elaborate and difficult chemical, microscopic and bacteriologic examinations of urine, stools, blood, spinal fluid and glandular secretions, of tests of metabolism rate, and, perhaps most important of all, the observation and consultation of several experts in special lines, before the pediatrician can arrive at a correct diagnosis. Such a study could be carried out in the home, if at all, only at an expense which is prohibitive for any but the very rich.

The trial of various methods of treatment in order to finally determine that method which is most effective in a particular case can be much more readily conducted in a well-equipped hospital, although oftentimes, once the best therapeutic procedure has been decided upon, the further treatment can be continued in the home to as great or even better advantage than in the hospital.

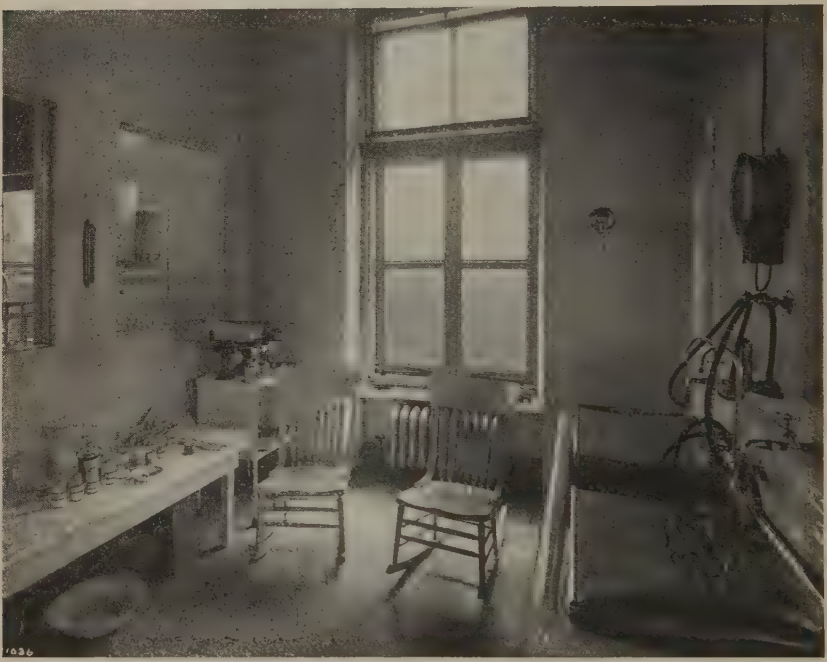


Fig. 131.—Infants' bath room, Sarah Morris Hospital for Children, Chicago, Ill. Water warmed bath trays, recording thermometer, casement windows, double transoms, partition windows and absence of wood architraves. (Richard E. Schmidt, Garden and Martin, architects.)

The children of the poor constitute by far the largest proportion of the patients in hospitals for infants and children, and thousands of young lives are annually saved which would inevitably be lost were they obliged to spend the period of their illness in the conditions obtaining in their homes.

That the conditions for surgical operations, in all but the simplest procedures, are far more favorable in a well-conducted hospital than in the home is so obvious as to need no argument.

And finally the consignment of children ill with contagious diseases to a properly arranged and efficiently conducted isolation hospital, or the contagious wards of any children's hospital, not only secures for the sick child much better chances for recovery, but protects other children in the family and neighborhood from the danger of infection and shortens the period of quarantine and detention from school of these children.

Other Functions.—The children's hospital (or the children's wards of a general hospital) has other functions than the care and cure of the patients.

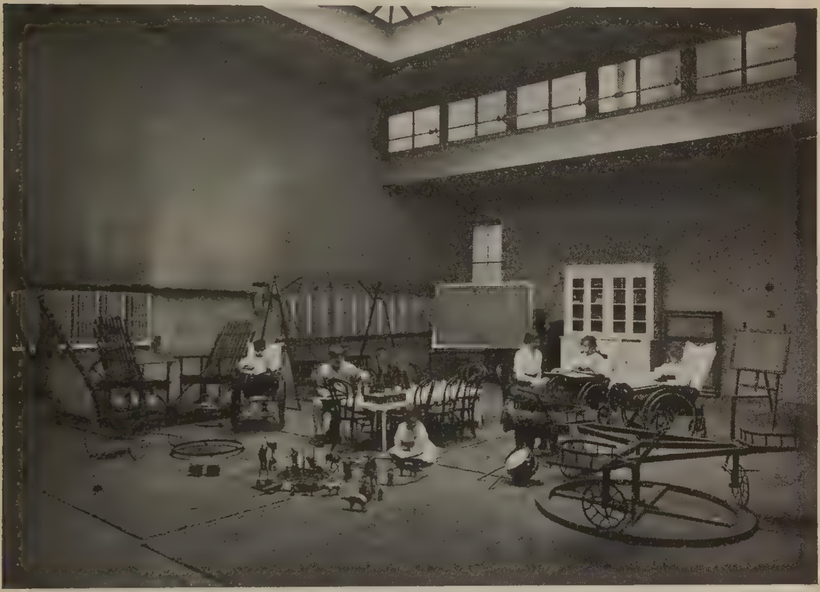


Fig. 132.—Play room, Sarah Morris Hospital for Children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

II. Instruction must be given and training afforded for the internes of the hospital, and, where possible, for students of medicine, who can acquire in no other way than by first-hand contact with sick children that knowledge and training which will make them safe practitioners of medicine.

III. The nurses of the hospital must be instructed to fit them properly for their duties in the hospital and for later service to the community.

IV. The importance of the social service worker has been abundantly established since the inauguration of this type of work in 1905 by Dr. Richard Cabot, and in no class of patients are the opportunities for usefulness greater than in Pediatrics. She, too, must be trained for service in the wards and the outpatient department of the children's hospital.

V. One of the most important functions of such a hospital is the instruction of mothers in the proper methods of the feeding and the care of their infants. No children's hospital is performing its full duty unless it has an infant welfare clinic, and, when possible, a nutrition clinic for older children.

VI. And, finally, the medical staff of every hospital should be seeking, constantly, to add to the world's stock of knowledge by the methods of thorough, accurate scientific investigation of the clinical material under their observation. Research, in a word, is an essential function of the hospital.

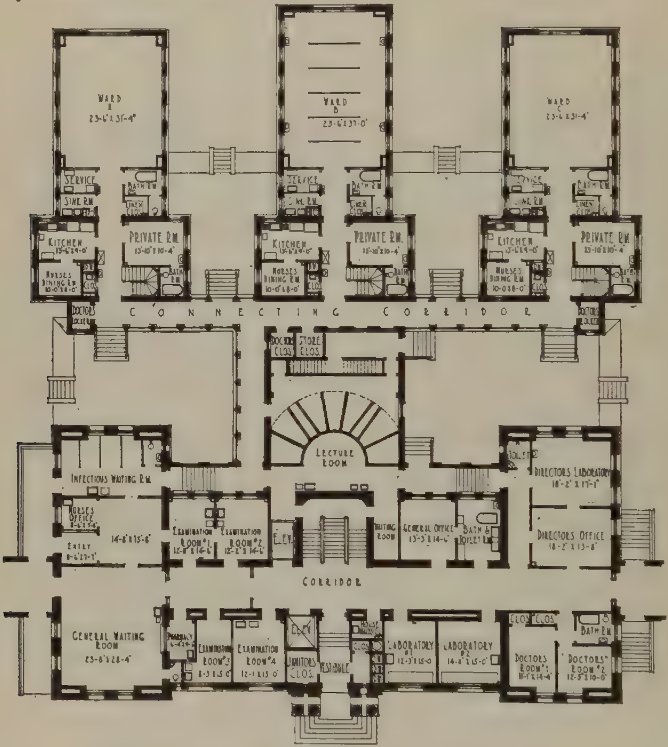

WARD A 23-6'x31-4"
WARD B 23-6'x37-0'
WARD C 23-6'x31-4'
SERVICE
SINK RM
BATH RM
LINEN CLOS
KITCHEN 13-6'x19-0'
PRIVATE RM 13-10'x10-4'
NURSES DINING RM 10-0'x8-0'
CLOS
DOCTORS LOCKER
C O N N E C T I N G C O R R I D O R
DOCTORS CLOS
STORE CLOS
LECTURE ROOM
INFECTIOUS WAITING RM
NURSES OFFICE
ENTRY
14-8'x15-6'
EXAMINATION ROOM #1 12-8'x14-6'
EXAMINATION ROOM #2 12-2'x14-6'
ELEV
WAITING ROOM
GENERAL OFFICE 13-3'x14-6'
BATH & TOILET RM
TOILET
DIRECTORS LABORATORY 18'-2'x17-1"
DIRECTORS OFFICE 18-2'x13-8'
CORRIDOR
GENERAL WAITING ROOM 23-6'x28-4'
PHARMACY
EXAMINATION ROOM #3 8-3'x15-0'
EXAMINATION ROOM #4 12-1'x15-0'
ELEV
JANITORS CLOS
VESTIBULE
HOUSE MAIDS
LABORATORY #1 12-3'x15-0
LABORATORY #2 14-8'x15-0'
CLOS
DOCTORS ROOM #1 11-5'x14-4'
DOCTORS ROOM #2 12-5'x10-0'
BATH RM

FIG. 133.—First floor, Harriet Lane Home for Invalid Children, Baltimore, Md. (Wyatt and Nolting—Butler and Rodman, associate architects.)

The functions of teaching these several groups, and of medical research, so far from being incompatible with the primary function of the hospital, the care and cure of the sick consigned to it, are certain to insure better and more adequate service for its patients than could be obtained in any other way. It is a safe statement that those hospitals which render the most modern, thorough and efficient service to their patients are those in which instruction is being given and original research is carried on by members of its medical staff.

The Inauguration of Children's Hospital Service in a Community—Plan of Procedure.—The first step in the matter of providing hospital service for any community—urban or rural— is to estimate the hospital needs in terms of number of beds. Such an estimate can never be other than approximate and this is conspicuously true of beds for infants and children. It is roughly estimated that, on the average, there is need for hospital beds in any community in the ratio of one bed for each 100 of the population. This is at present in excess of the actual needs, except in times of severe epidemics, and greatly in excess of the actual provision of beds in the United States. A survey of the hospitals of this country made by the Council on Medical Education and Hospitals of the American Medical Association in 1920–1921, and reported in the issue of the Journal of the American Medical Association for Apr. 6, 1921, found the grand average of hospital beds to be one for 340 of the population. The list of hospitals investigated includes private, general and special hospitals caring for patients with acute and subacute diseases, but does not include state institutions which are devoted largely to custodial care of tuber-

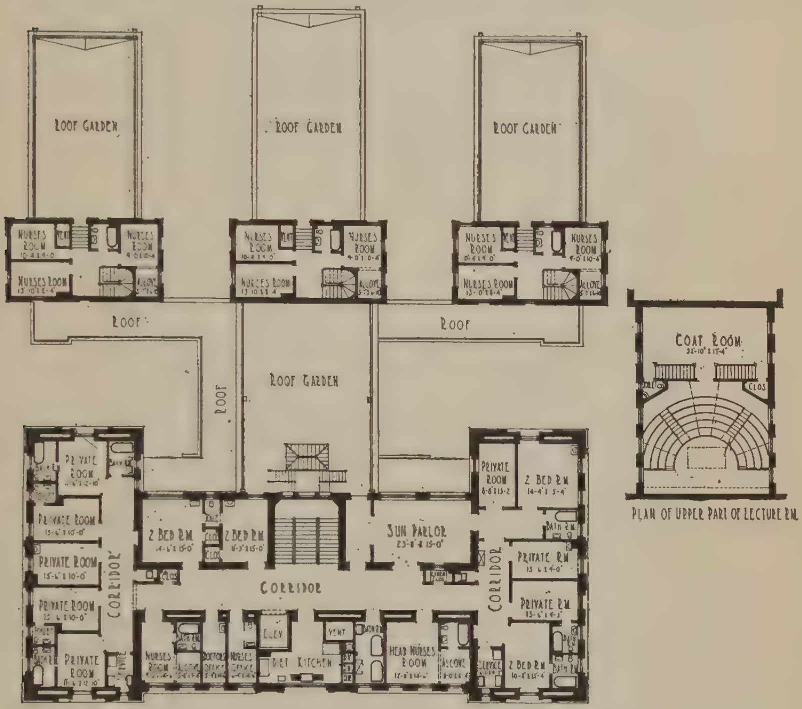
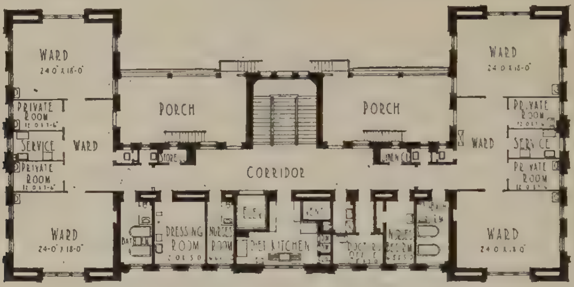


FIG. 134.—Second floor, Harriet Lane Home for Invalid Children, Baltimore, Md. (Wyatt and Nolting—Butler and Rodman, associate architects.)

culosis, incurable nervous or insane patients; nor homes for deaf, blind, crippled or aged persons; nor prison or school hospitals (unless such hospitals are clearly distinguished from the prisons or schools), nor the hospitals controlled by the U. S. Army, Navy or Public Health Service. The ratio of beds varies widely in different parts of the country from one bed for every 139 people, in Arizona, one bed for every 185 in New York, to one for every 1,054 persons in Mississippi.



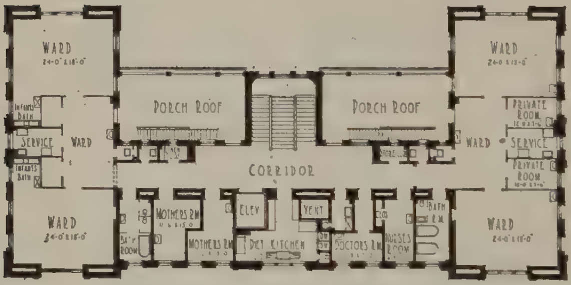


FIG. 135.—Fourth floor, Harriet Lane Home for Invalid Children, Baltimore, Md. (Wyatt and Nolting—Butler and Rodman, associate architects.)

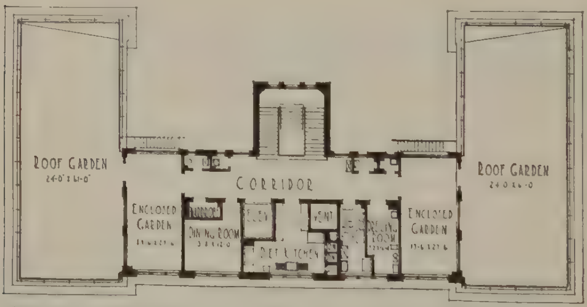


FIG. 136.—Fifth floor, Harriet Lane Home for Invalid Children, Baltimore, Md. (Wyatt and Nolting—Butler and Rodman, associate architects.)

What proportion of hospital beds should be set aside for infants and children is not readily determined, because the needs vary widely

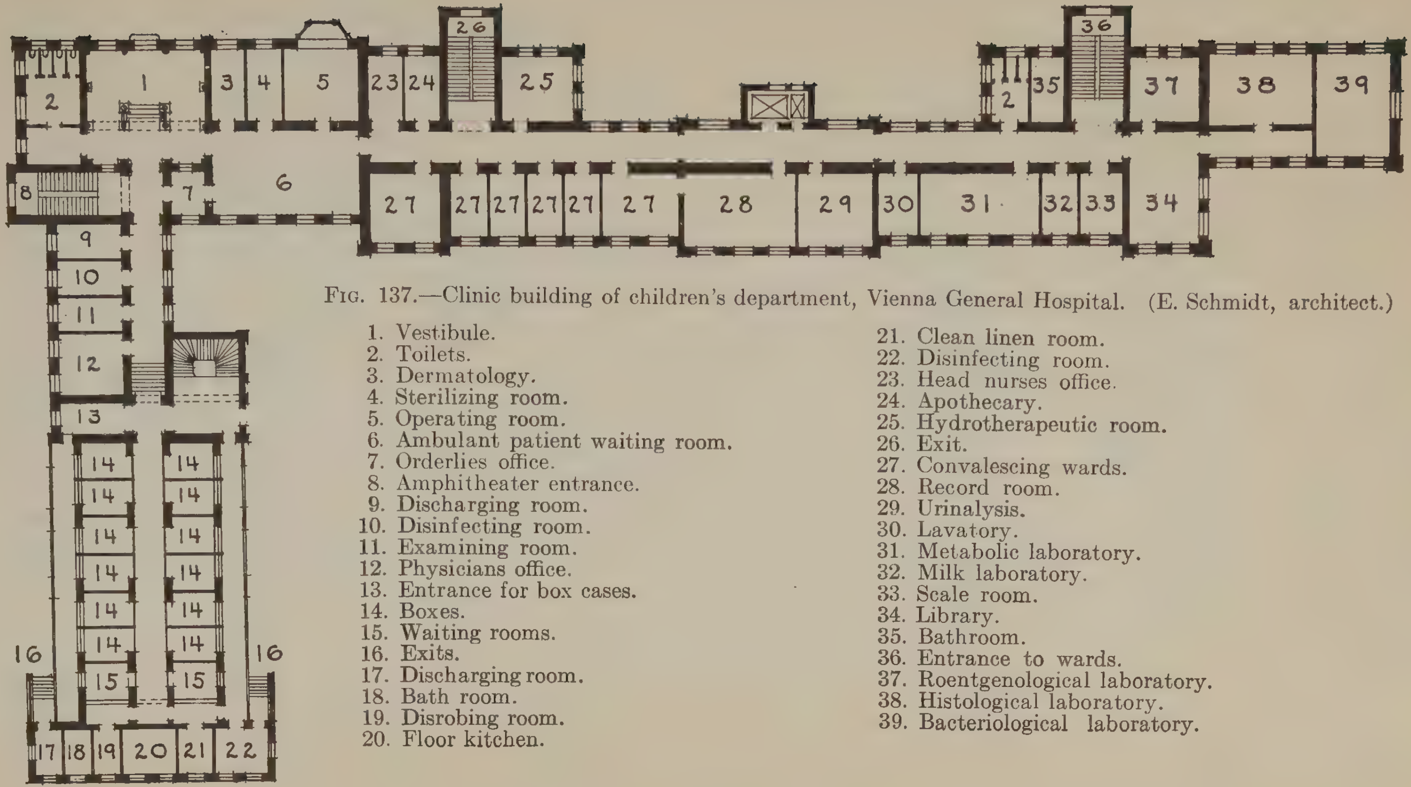


FIG. 137.—Clinic building of children's department, Vienna General Hospital. (E. Schmidt, architect.)

1. Vestibule.
2. Toilets.
3. Dermatology.
4. Sterilizing room.
5. Operating room.
6. Ambulant patient waiting room.
7. Orderlies office.
8. Amphitheater entrance.
9. Discharging room.
10. Disinfecting room.
11. Examining room.
12. Physicians office.
13. Entrance for box cases.
14. Boxes.
15. Waiting rooms.
16. Exits.
17. Discharging room.
18. Bath room.
19. Disrobing room.
20. Floor kitchen.
21. Clean linen room.
22. Disinfecting room.
23. Head nurses office.
24. Apothecary.
25. Hydrotherapeutic room.
26. Exit.
27. Convalescing wards.
28. Record room.
29. Urinalysis.
30. Lavatory.
31. Metabolic laboratory.
32. Milk laboratory.
33. Scale room.
34. Library.
35. Bathroom.
36. Entrance to wards.
37. Roentgenological laboratory.
38. Histological laboratory.
39. Bacteriological laboratory.

in different communities and at different times, depending on the type of population, whether industrial or agricultural, rich or poor, and there is, of necessity, a sharp increase in the demand for beds in times of severe epidemics. In the cities of the United States in which the demands for such hospital service for children seem to be met with reasonable adequateness, the ratio of children's beds is about one to 2000 of the population, not including those in homes and asylums designed primarily for the housing of children who are not sick. A wise plan is to provide, primarily, for such number of beds as are decided to be necessary in the conjoint opinion of the physicians in the community, but on a plan of room and ward construction which will admit of ready expansion to meet increasing needs, particularly in times of epidemics of contagious diseases.

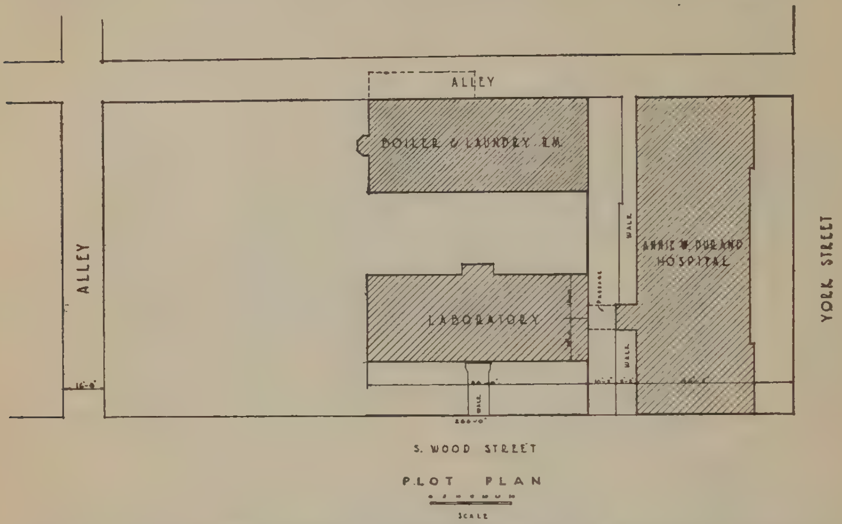


FIG. 138.—Plot plan, Annie W. Durand Hospital of the John McCormick Memorial Institute for Infectious Diseases, Chicago, Ill. (Chas. S. Frost, architect.)

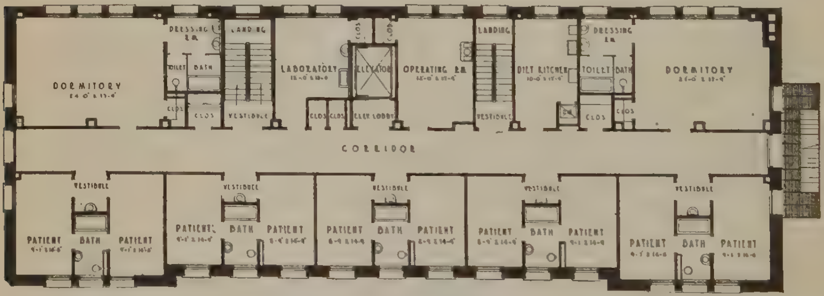


FIG. 139.—Third floor, Annie W. Durand Hospital of the John McCormick Memorial Institute for Infectious Diseases, Chicago, Ill. (Charles S. Frost, architect.)

A Children's Hospital or Children's Ward in a General Hospital.—Will the needs of sick infants and children be best met by a hospital exclusively devoted to them, or by the provision of special wards and rooms in a general hospital? When there is need for a children's hospital of sufficient size there is decided advantage in an institution devoted exclusively to this class of patients. On the other hand, it is wasteful and uneconomic to maintain a small hospital, less than 75 to 100 beds, for any purpose, although, of necessity, in

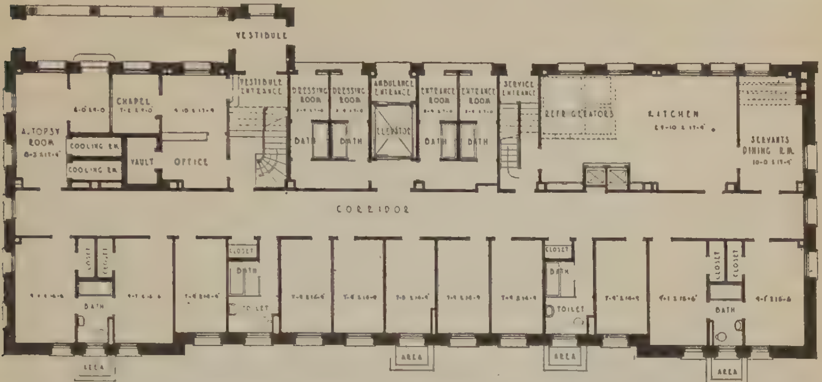


FIG. 140.—Ground floor, Annie W. Durand Hospital of the John McCormick Memorial Institute for Infectious Diseases, Chicago, Ill. (Charles S. Frost, architect.)

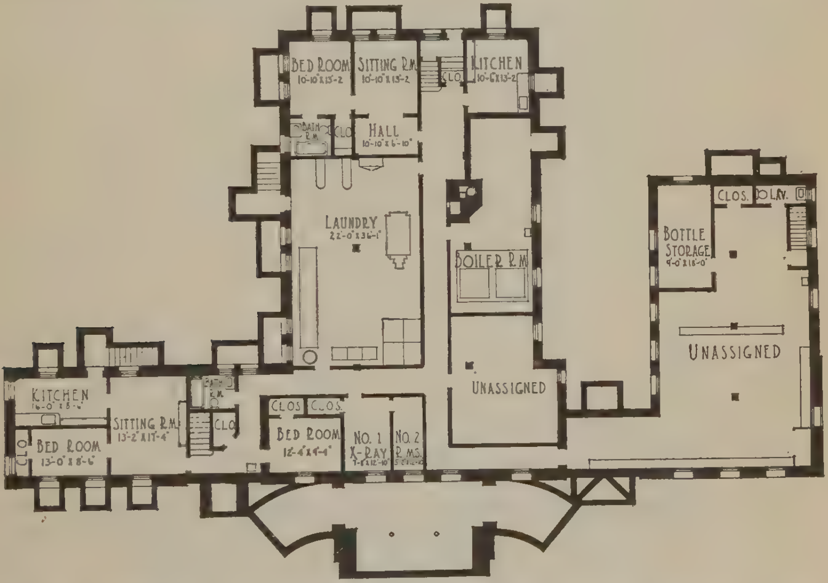


FIG. 141.—Basement, The Babies' Dispensary and Hospital, Cleveland, Ohio. (Abram Garfield, architect.)

smaller cities and rural districts the one hospital to serve all needs must be smaller than this. In general it may be said that if the demand for beds for infants and children does not total at least 75, it is better to

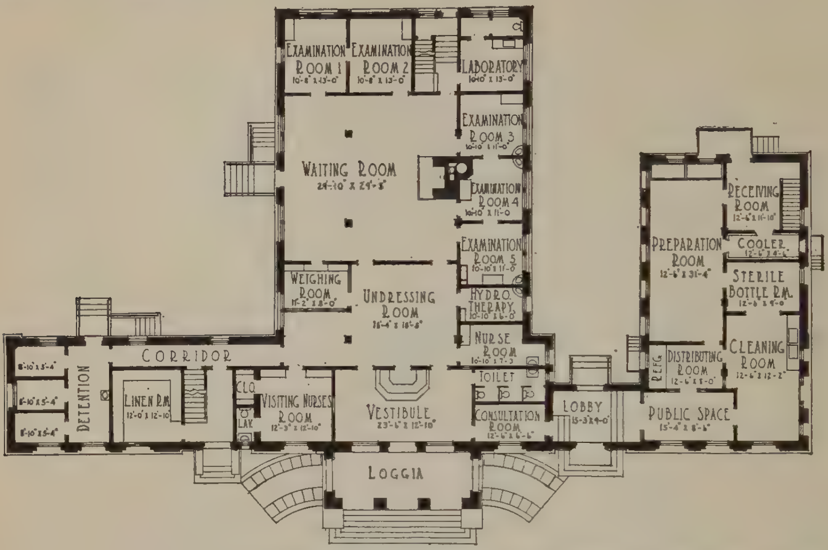


FIG. 142.—First floor, The Babies' Dispensary and Hospital, Cleveland, Ohio. (Abram Garfield, architect.)

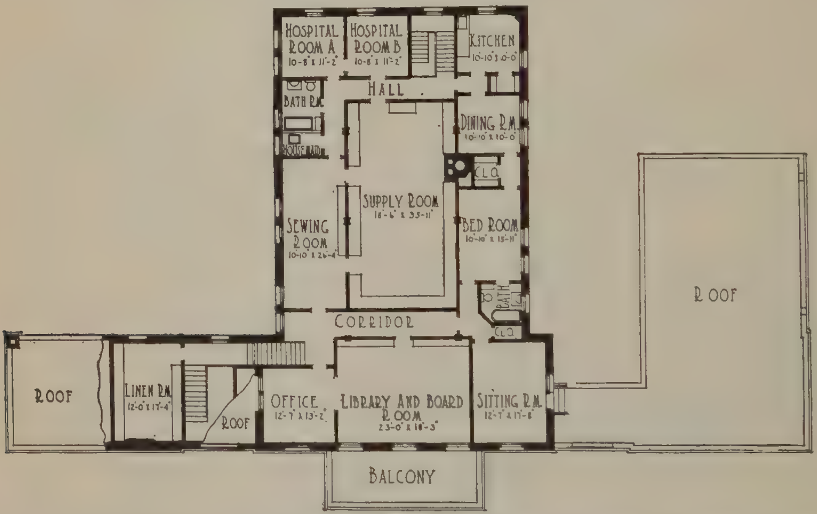


FIG. 143.—Second floor, The Babies' Dispensary and Hospital, Cleveland, Ohio. (Abram Garfield, architect.)

make special provision for these patients in a general hospital. The overhead expense for administration is not much greater for a hospital of 300 beds than for one of 50 beds, while, of course, the percentage of

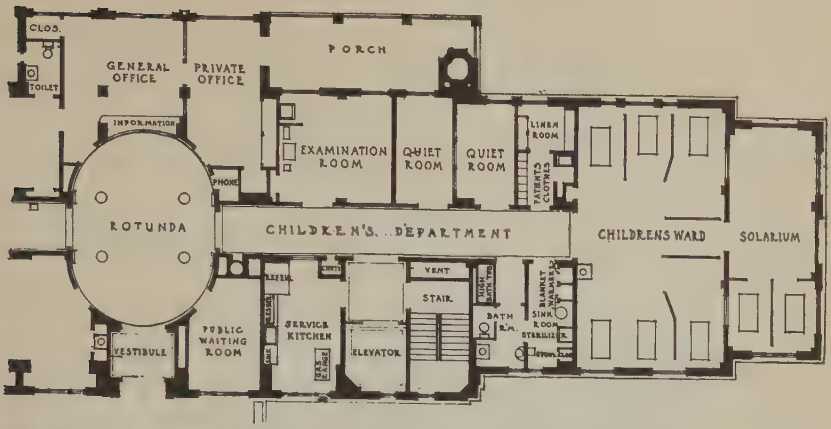


FIG. 144.—Children's ward, first floor, Carson C. Peck Memorial Hospital, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

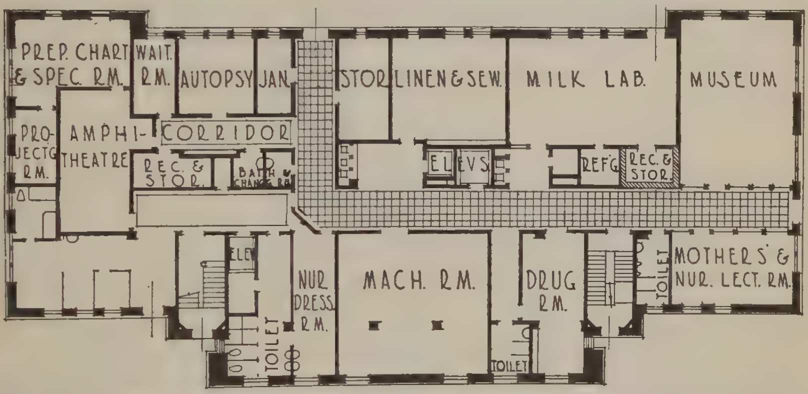


FIG. 145.—Basement, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

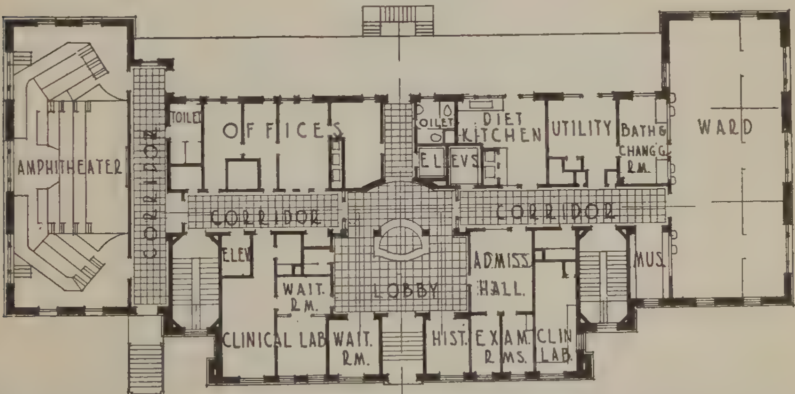


FIG. 146.—First floor, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

that cost per bed is very much larger in the smaller hospital. The per patient cost of administration expense in very many hospitals is enormous, so disproportionate to the total cost of maintenance, as would not be tolerated in any well-managed business enterprise.

It is necessary to consider, therefore, two methods of solution of the children's hospital problem, the hospital devoted solely to sick infants and children, and the infants' and children's wards of a general hospital.

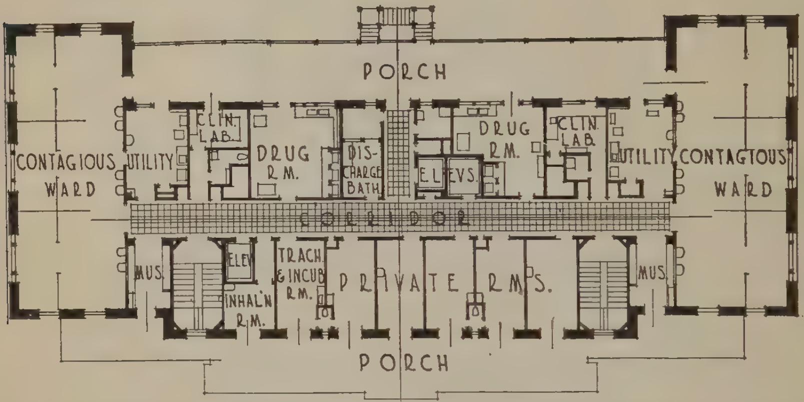


FIG. 147.—Second floor, Babies' and Children's Hospital of Cleveland, Cleveland Ohio. (Abraham Garfield, architect.)

Before considering these two alternatives, however, it will be well to consider the types of hospitals in general in respect to the control and the provision for the cost of erection and maintenance.

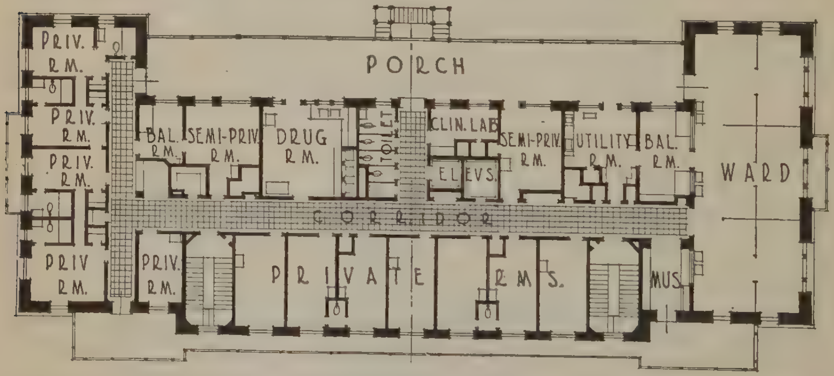


FIG. 148.—Third floor, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

Hospitals may be established as (1) Public Hospitals (Federal, State, County or Municipal), or (2) as Private Hospital (incorporated *not* for profit, or incorporated for profit). The private institutions *not* conducted for profit are maintained by religious sects, fraternal orders, benevolent societies or other groups of like character. Those conducted for profit are owned usually by a single individual, by a corporation, for example, a medical school, or by a group of practitioners.

In theory the public hospital, erected by the city or community as a whole, controlled by a Board of Trustees or Directors, elected or appointed and responsible to the community, supported by public funds appropriated for that purpose, would seem the ideal method of providing for the care of the indigent sick. Practically, there are serious objections to such a plan in all but the largest cities, and even in such places, the history of public hospitals in the United States has been far from ideal. The temptation on the part of the public officials to allow politics to enter into the conduct of such a hospital, in the selection of officials, employees, and even of the medical staff, thus subverting the function of the institution from its real purpose as a

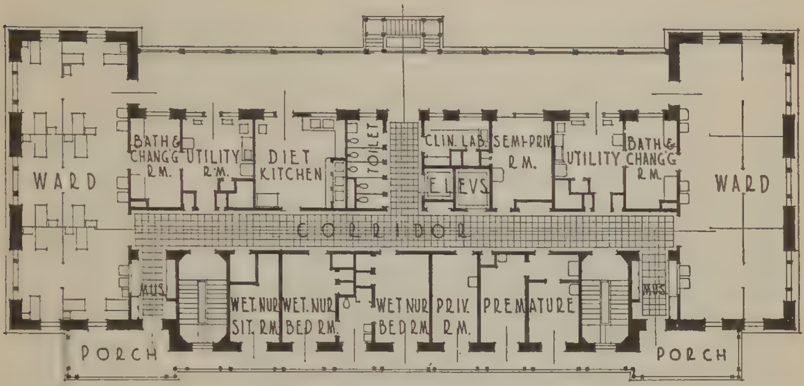


FIG. 149.—Fourth floor, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

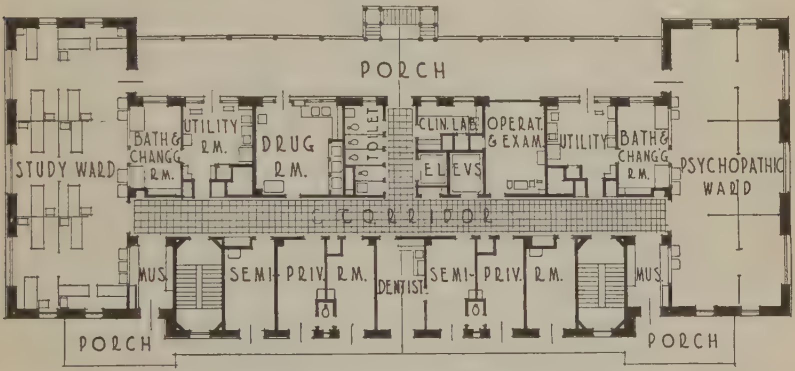


FIG. 150.—Fifth floor, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

place for the most efficient care of the sick, is apparently too great to be resisted by those in authority. Possibly, in time, those who seek and attain political control in our municipalities will learn that it is good politics, redounding in the long run to their political advantage, to conduct such an institution as a hospital with sole reference to its real purpose.

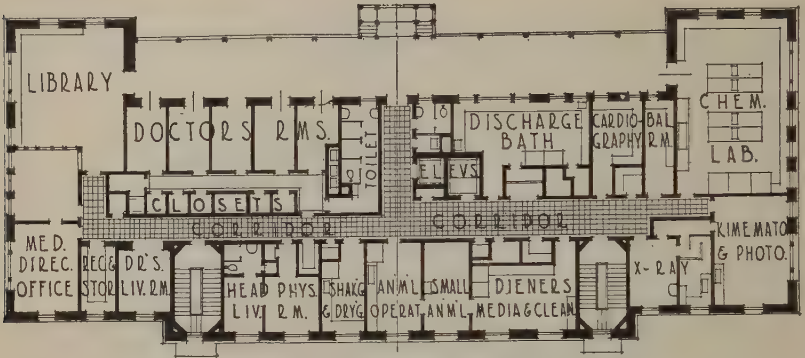


Fig. 151.—Sixth floor, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

The second objection to purely public hospitals is the fact that in the smaller cities provision must be made in one institution for the care of pay as well as pauper patients, and it is not a proper function of a municipality to conduct a hospital as a business for profit, as such an institution, in part, must be conducted.

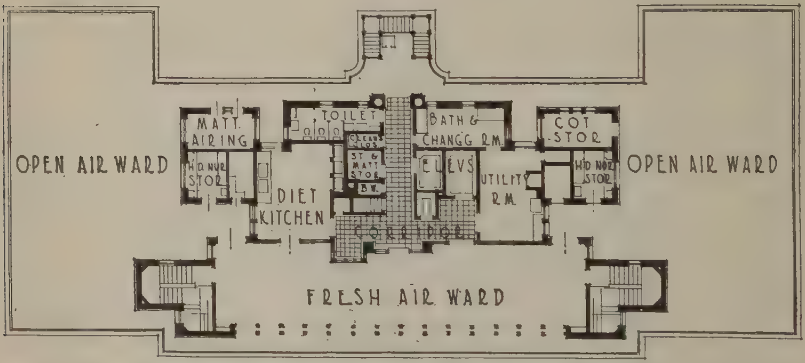


Fig. 152.—Plan of roof ward, Babies' and Children's Hospital of Cleveland, Cleveland, Ohio. (Abraham Garfield, architect.)

For most communities, therefore, the better plan is a private hospital conducted *not* for profit, erected and maintained by private contributions, managed by a board of trustees, directors, governors or managers, selected by the corporation, which, in turn, is composed of all persons contributing any considerable sums to the support of the hospital. Free beds for the indigent sick are supplied by endowment, or from city funds appropriated for that purpose, or in both ways.

The great majority of hospitals in the United States are of this type, but most of them have been organized by groups of persons united by some common tie, usually that of a religious sect, and so our hospitals are in large part Baptist, Catholic, Episcopalian, Jewish, Methodist, Presbyterian or representative of some other religious sect. The world owes a great debt to these church organizations which have made

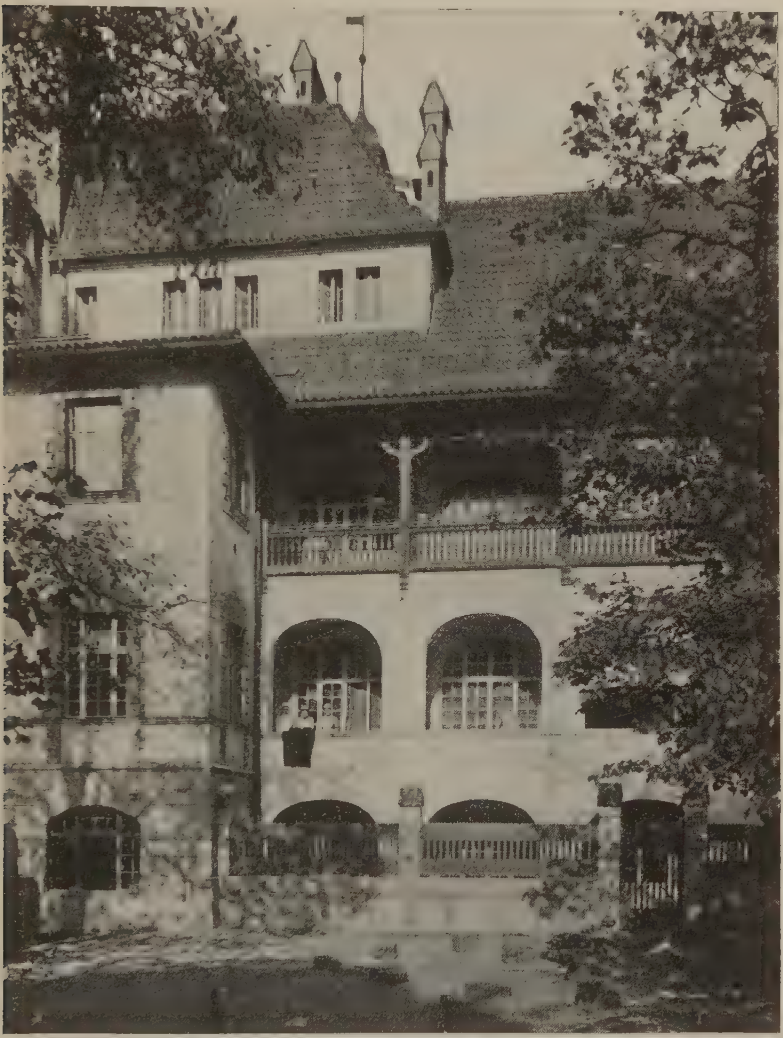


FIG. 153.—Municipal Children's Asylum and Hospital, Berlin, Schmidt-Gallisch Foundation. (Ludwig Hoffmann, architect.)

provision for the care of the sick, which would doubtless not have been secured so soon through any other agency. In a large city, where there is need of many hospitals, there are many advantages and fewer objections to this plan. In the smaller communities, however, where a single hospital is all that is needed, it seems obvious that a hospital controlled by an organization in which all of the religious sects and other community groups are united in a hospital scheme, non-sectarian in character, and conducted as a community hospital, must command the whole-hearted support of all citizens of that community as can no hospital controlled by a single sect or faction.

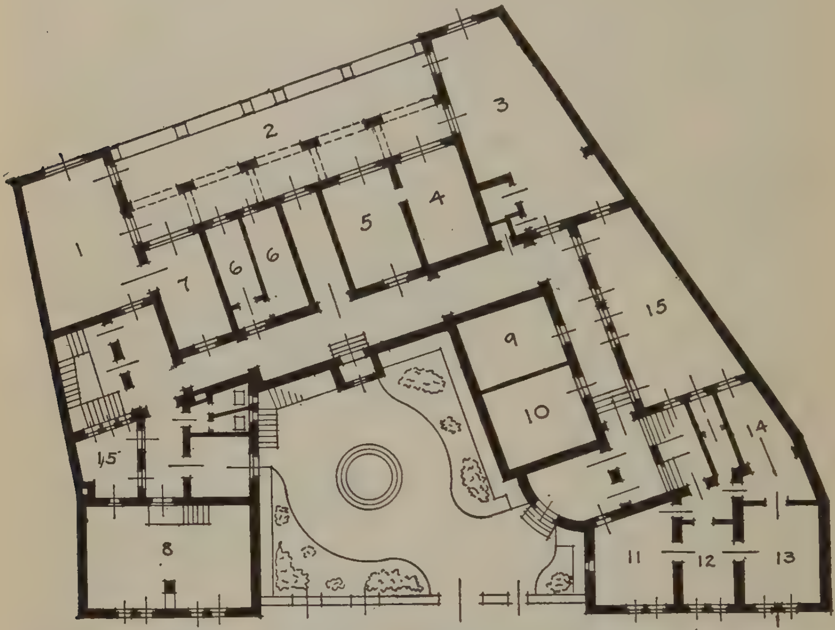


Fig. 154.—Children's Asylum and Hospital, Berlin, Schmidt-Gallisch Foundation. 1, Kitchen; 2, plat yard; 3, laundry; 4, dryingroom; 5, ironing and repairing; 6, pantries; 7, scullery; 8, heating apparatus, 9, mangle room; 10, linen room; 11, 12, 13 and 14, janitor's quarters; 15, courts. (Ludwig Hoffmann, architect.)

Governing Board.—The hospital corporation, made up of all persons who have made any considerable contribution to the hospital (the larger the number the better), elects a Board of Directors, or Trustees, or Managers, or Governors (whichever term is preferred), and to this Board is delegated the authority to conduct the institution. This Board is held responsible for the proper and efficient management of the institution, and to secure good results must be given full authority in the appointment and control of those persons whom it appoints to conduct the work. The Board should be not too large in number, preferably from 7 to 15. The members should be elected solely with reference to their ability and willingness to give the necessary time to the direction and control of the hospital, and their ability to bring knowledge and experience to the several phases of hospital management, not because it is hoped that some persons of wealth may be induced to give a larger sum to the institution if he is made a director or trustee. The terms of service of each member of the board should be three, five or more years and the time of re-election so arranged that the term of office of not more than one or two members expires in any one year. For example: At the first election of a board of 15 trustees three are elected for a term of one year, three for two years, three for three, three for four and three for five years. Thereafter, three members are elected annually as vacancies occur. Such a plan insures the presence at all times of a majority of members who have had considerable experience.

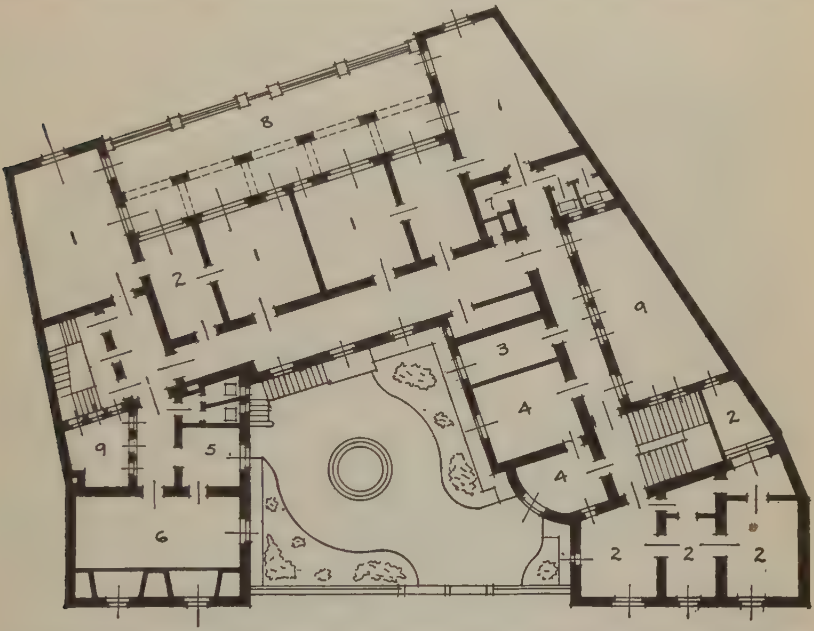


Fig. 155.—Children's Asylum and Hospital, Berlin, Schmidt-Gallisch Foundation. 1, Wards; 2, nurses' rooms; 3, floor pantry; 4, internes' rooms; 5, laboratory; 6, day room; 7, elevator; 8, veranda; 9, courts. (Ludwig Hoffmann, architect.)

The Board is organized by the election of the usual officers, a President, a Vice-president, a Secretary and a Treasurer, although the Secretary and Treasurer can often with advantage be united in one person. The duties of these officers are the same as usually obtain in the Board of Directors of any corporation or company. The office of president is the most important and selection of the incumbent should be made with special care. He is the usual medium of contact between the corporation, the Board of Directors and the Superintendent, the medical staff and other persons actively engaged in the work of the hospital.

The Board should hold meetings with sufficient frequency (at least once in three months) to enable its members to keep closely in touch with the work of the institution.

Women's Auxiliary Board.—Many hospitals have found it of advantage to have an auxiliary board of women, keenly interested in the institution and rendering service by supplying linen, clothing, dainties, books, flowers, entertainments and other items which contribute to the comfort and happiness of the patients. Where such a women's board is established its functions should be clearly defined and understood, that there may be no conflict of authority with the Board of Directors.

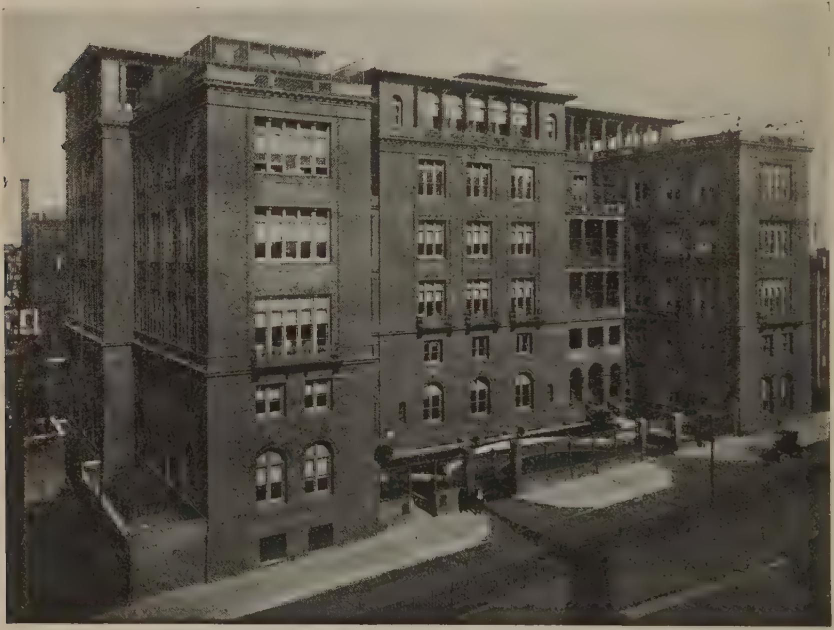


Fig. 156.—Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

Conduct of the Hospital.—The immediate work of the hospital devolves upon persons appointed by the Board of Directors for that purpose, and who are competent, by reason of experience, training and demonstrated capacity for their several duties, who are, in other words, expert in their several lines.

The most important of these officials are the members of the Attending Medical Staff, the Superintendent and the Director or Superintendent of Nurses or of the School for Nurses, if such there be. These officers should be selected with great discrimination, and there is advantage in appointing the Superintendent and the leading members of the medical staff before plans for the hospital, or even its location, are decided upon. These persons, presumptively, have expert knowledge of at least many phases of hospital work and their advice should be of value. Moreover, they will enter more eagerly and happily into the work of an institution in the planning of which they have had a voice.

The Medical Staff.—The fundamental purpose of a hospital is to make the sick well, to relieve suffering and prolong life. Therefore, the most vital feature of its organization is the group of men who render medical service to the patients within its walls. Efficient conduct of the business of the hospital, good nursing, social service and the like are all helpful and necessary aids, but they are adjuncts only and fail of their purpose unless intimately correlated with and subordinate to the work of the physicians of the staff. The success of any hospital depends more than on all else on the character and devotion of the medical staff.

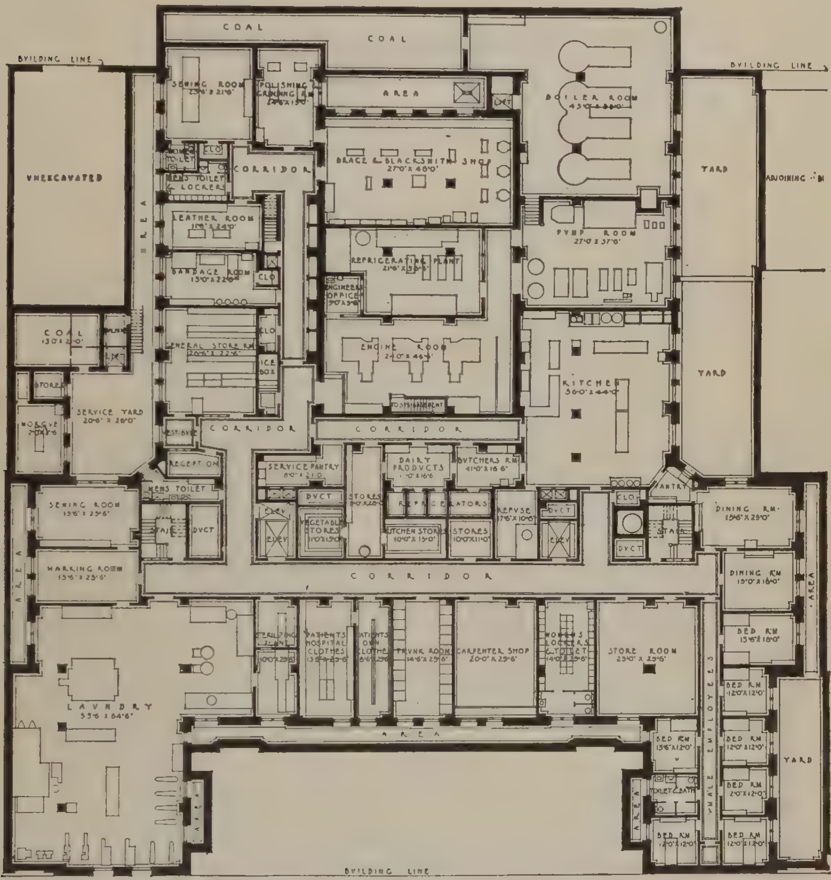


FIG. 157.—Basement, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

Such a staff usually comprises the following groups. Consulting, Attending, Associate and Resident.

Attending Staff.—It is universally agreed that to secure the best results a hospital must have an organized, responsible Attending Staff, as few in number as possible to care for the ward patients, and on which are included physicians who are expert in the several special branches of medicine represented by the diseases which afflict the patients admitted to its beds.

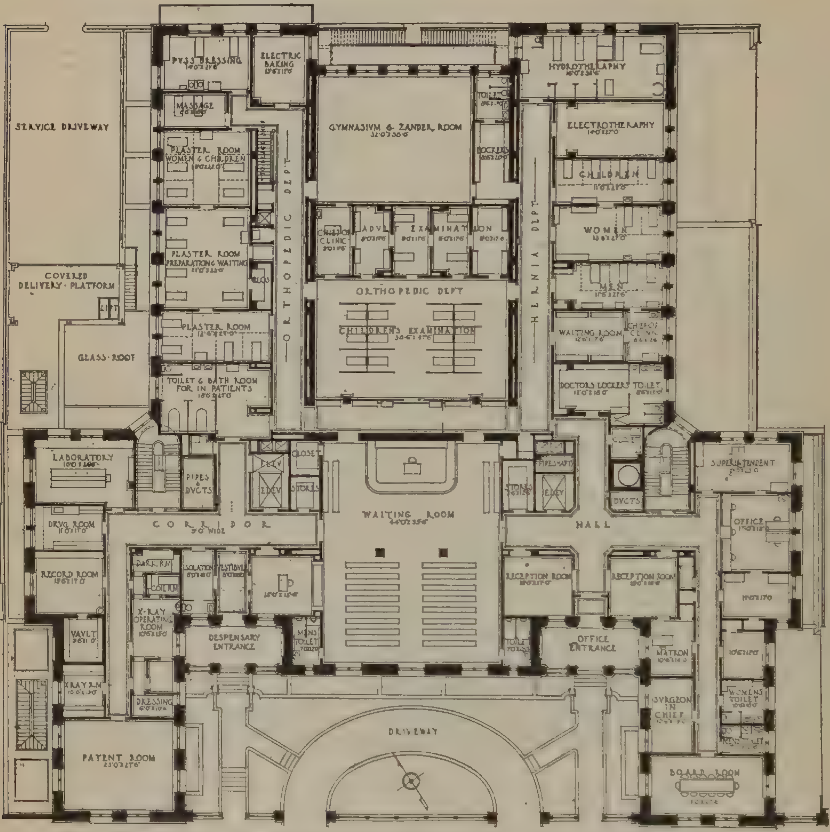


FIG. 158.—First floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

In a hospital for children such a list would include pathology, medicine, neurology, surgery, orthopedics, oto-laryngology, ophthamology, dermatology and roentgenology. The staff should be made up of at least one representative of each of these divisions of medicine, the number in each group being increased when the number of patients is too large for one physician to render the required service. Appointments should be made solely on the basis of merit, preferably, in a large hospital, by means of a Civil Service examination in which due weight is attached to experience and previous accomplishment. The appointment should be for fairly long term, 5 to 10 years, and the service continuous. The plan of dividing a service into three, four or six month periods, the attending physician in each division alternating terms of work, has not proven satisfactory. To this attending staff is delegated the responsibility for the medical work of the hospital. They are appointed by the Board of Directors and vacancies occurring at any time by death, resignation or removal for cause are filled in the same manner.

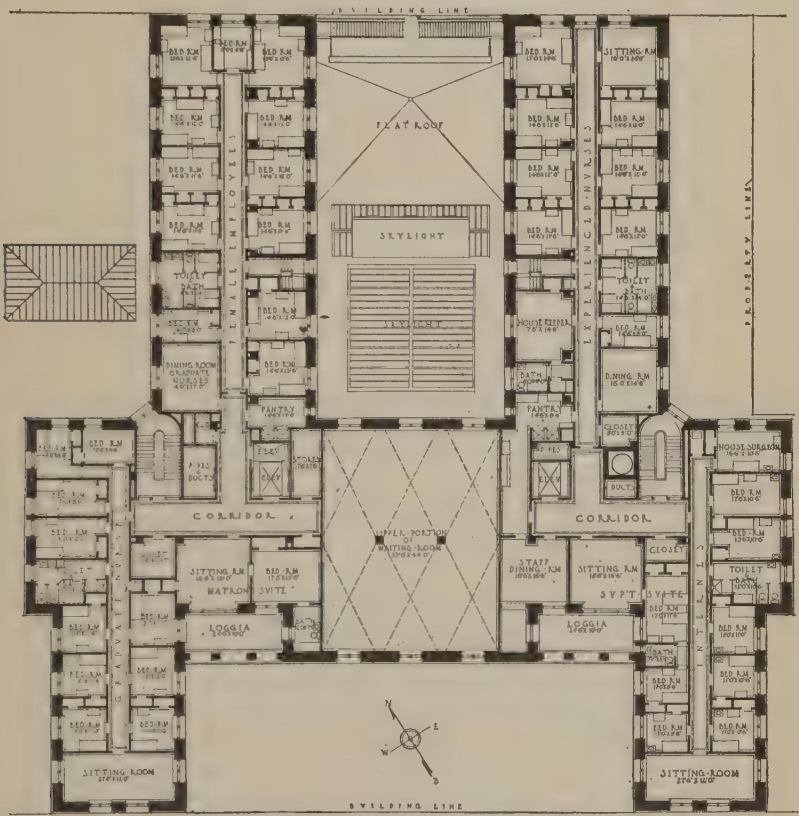


FIG. 159.—Second floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

Consulting Staff.—The Consulting Staff is made up, usually, of former members of the Attending Staff who have retired from active work in the hospital, but who may be called in consultation in difficult cases where their advice is desired, or it may include other physicians in the community of large experience and special ability.

Associate Medical Staff.—In cities of moderate size, where the number of physicians in practice is larger than can be included in the Attending Staff, it is essential to make provision whereby these physicians can have the advantages of a hospital for the care of their patients. The hospital, moreover, should have its beds occupied to as near capacity as possible, all of the time, for economic reasons and in order that it may be of the utmost usefulness to the community. For this reason very many hospitals in this country have been and still are conducted without any official medical staff, their rooms and wards being open to patients of any physician by whom they may be referred. This is not a safe nor a satisfactory plan. No group of persons in control of a hospital can be indifferent to the nature of the service rendered by the institution. They cannot wish to sanction the work of incompetent or dishonest medical men, yet they are not as a rule able to distinguish such incompetents, and even when they are able to do so, it is not easy, in the absence of a responsible medical staff, to exclude such physicians from the privileges of the hospital. An admirable plan to meet the needs of the community and at the same time exercise a control over the selection of physicians who are admitted to the privileges of the

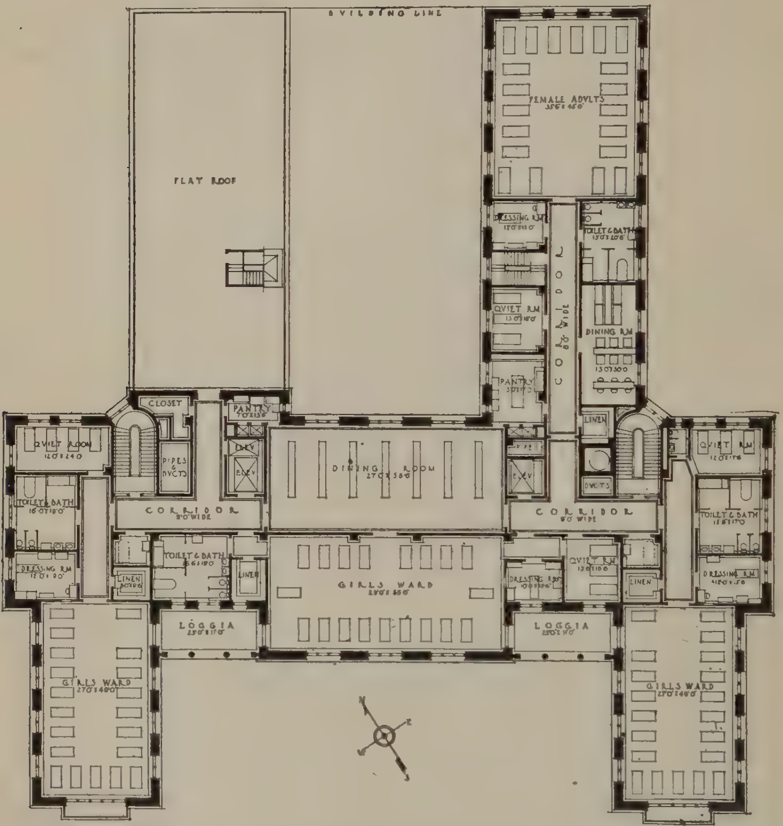


Fig. 160.—Third floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

institution is through the appointment of an Associate, Adjunct or Visiting Staff, appointed by the Board of Directors on nomination of the Attending Staff which is held responsible therefor. Such a staff may be quite large, and include, in a small city, practically all of the physicians of known ability and integrity. The members of this staff have at their command all of the resources of the institution for the patients whom they consign to it, either in private rooms only, or in both wards and rooms as may be agreed upon by the Directors. The Board should reserve the right of dismissal of any member of the Associate Staff for cause. From its members the Attending Staff may be from time to time recruited.

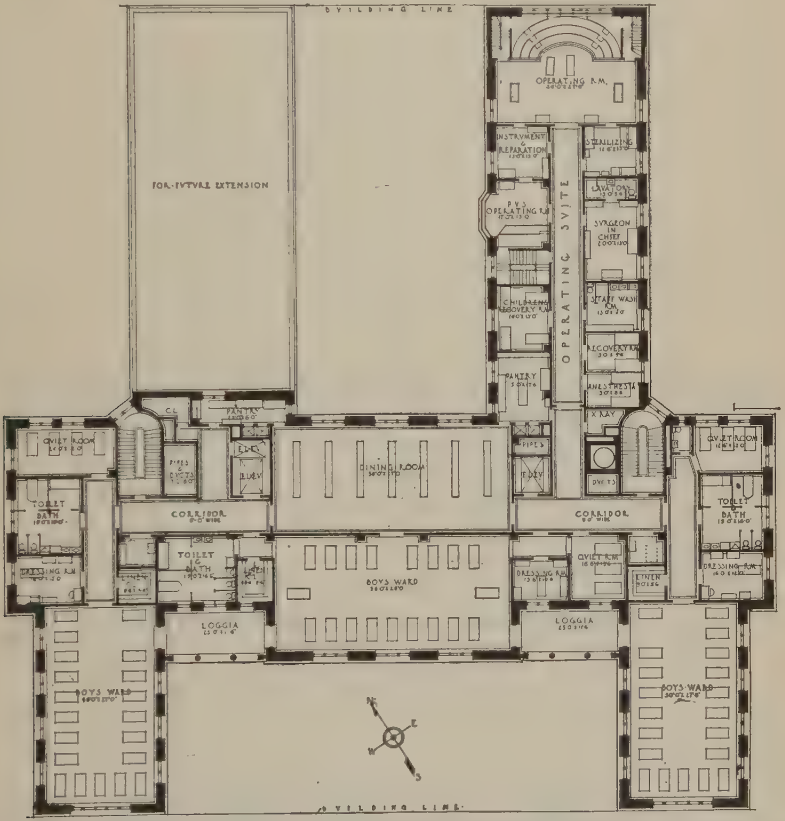


FIG. 161.—Fourth floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

The Resident Staff.—In all but very small hospitals, members of whose attending staffs are within prompt call at any time, there is need for one or more physicians who reside in the hospital, and are in immediate charge of the patients, under the direction of members of the Attending or Associate Staff, and whose services can be had at once in case of emergency. This Resident Staff consists usually of internes, for the most part recent graduates in medicine, and, in addition, in the larger hospitals, of one or more residents, e.g., a resident physician and surgeon, or one of each. These residents are men of longer experience than the interne, most frequently physicians who have served a year or more as internes and have been advanced to the rank of residents. Internes are selected either by competitive examination or by appointment on their record in the medical school and recommendations of their teachers and others who know them.

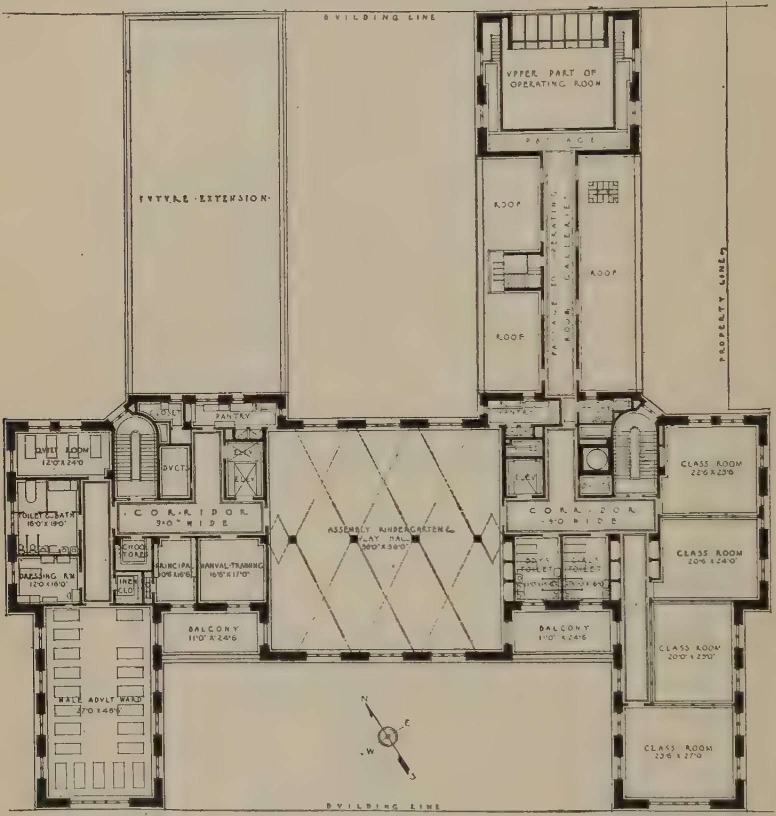


FIG. 162.—Fifth floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

A new feature has been added to the interne situation in recent years by the requirement of an interne year as a prerequisite for graduation in several of the medical colleges of the United States and as a requirement for licensure by a number of the State Medical Examining Boards. The regulations governing this interne year recognize service only in a *general* hospital, the service of the interne to include work in the several branches of medicine, surgery and obstetrics. Service in a special hospital, like one devoted to nervous and mental diseases, or diseases of the eye, ear, nose and throat, is recognized only for a portion, usually 3 months, of the required 12. This rule should not apply to hospitals for infants and children of such capacity that the several specialties are represented in the work of the institution. They offer as wide a range of experience as do hospitals for adults, with the exception of obstetrics. For experience in this branch of medicine the interne must take supplemental work in a Lying-in Hospital, as is the case with a large proportion of those serving in general hospitals, because many of these latter institutions have no obstetrical wards.

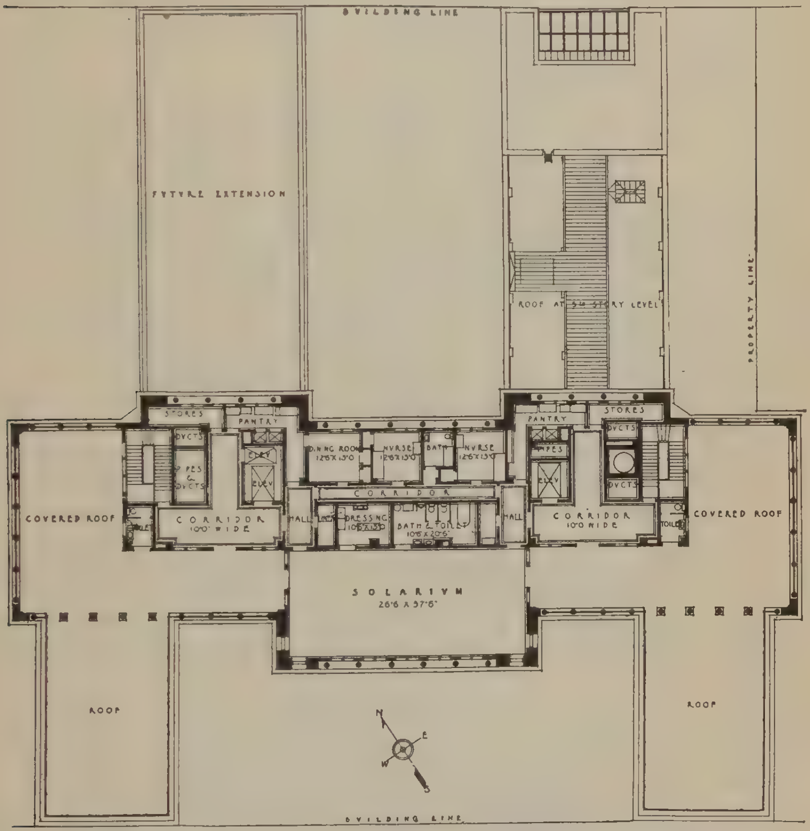


Fig. 163.—Sixth floor, Hospital for the Relief of the Ruptured and Crippled, New York City. (York and Sawyer, architects.)

The smaller children's hospitals must rely, for the most part, on resident physicians, meaning by this those who have already served as internes for a year or more in a general hospital, but who desire experience and training in pediatrics. Internes entering upon service in a children's hospital immediately after completion of the curriculum of the medical college usually receive only maintenance. Resident physicians of larger experience must, as a rule, be paid a salary, ranging from $25 to $100 per month in addition to maintenance.

A third group to which the children's hospitals may look for service as residents is composed of practitioners of medicine who seek post-graduate study and training in pediatrics. The rapid advance of this branch of medicine has led to a widespread demand by general practitioners for post-graduate instruction in this line. In no way can this be so effectively obtained as by service in a children's hospital under competent and experienced physicians who are devoting themselves exclusively to the diseases of infancy and childhood. In the absence of a sufficient number of recently graduated medical students to supply the needs of the children's hospitals, general practitioners desiring continuation study in pediatrics can render valuable service to these hospitals. The terms of service must, as a rule, be shorter than in the

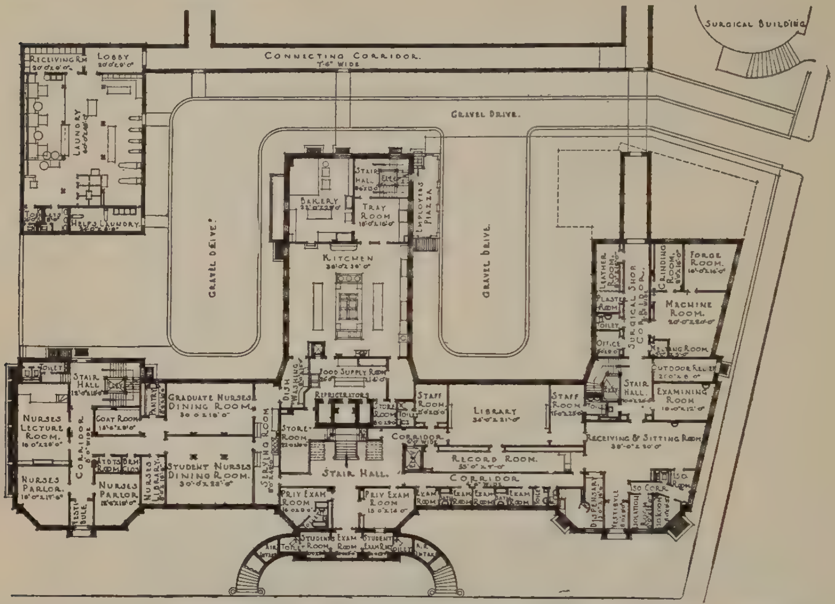


Fig. 164.—Ground floor, The Children's Hospital, Boston, Mass. (Shepley, Rutan and Coolidge, architects.)

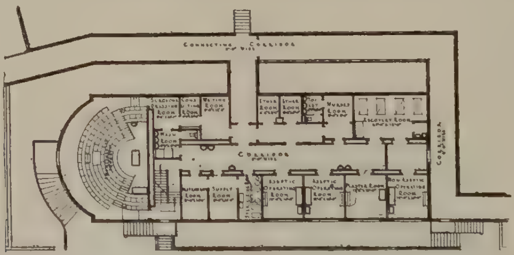


Fig. 165.—First floor, surgical building, The Children's Hospital, Boston, Mass. (Shepley, Rutan and Coolidge, architects.)

case of the usual internes, seldom, probably, over three or at most six months, because such a physician cannot well be absent from his own practice for a longer period.

The Hospital Superintendent.—The successful conduct of any hospital depends very largely on the superintendent. He is responsible for the conduct of the business of the hospital and must have intimate knowledge of all the phases of hospital activity other than those which are strictly medical. He engages and discharges directly (or, in a large hospital, through his subordinates) all employees, purchases supplies, and is directly responsible for the transaction of all business with the patrons of the hospital, for the enforcement of rules and regulations and for the physical condition of the grounds, buildings and equipment. The selection of the superintendent is, therefore, one of the most important tasks of the Board of Directors. Unfortunately, the demand for such officials far exceeds the supply. There is real need for the establishment of courses of training in hospital superintendency, designed to prepare men and women for this important and exacting vocation, more systematically and with less expenditure of time than by the apprentice system, if such it can be called, which is, up to the present time, the only method of training for such service. The successful hospital superintendent must be a person of energy, tact, patience and perseverance, with a thorough training in modern business methods, and with good administrative and executive ability. There

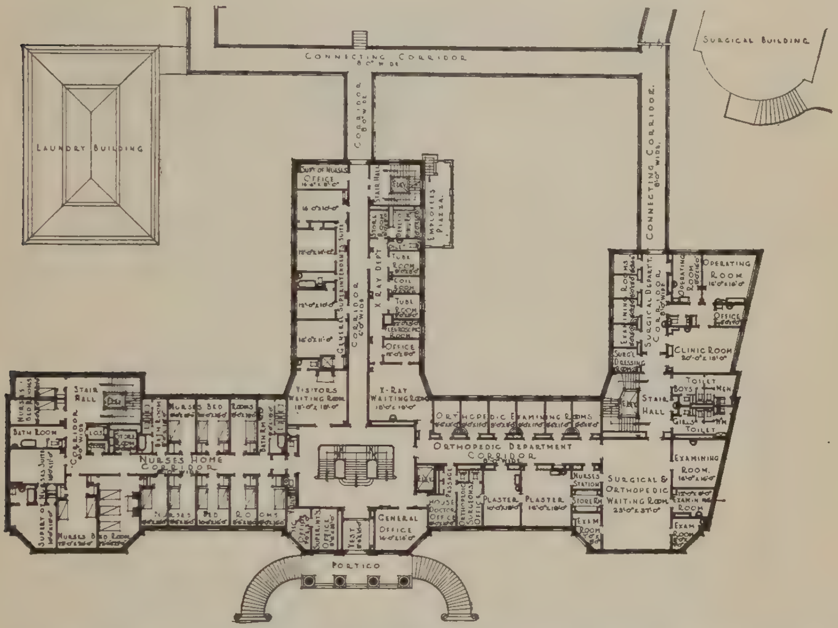


FIG. 166.—First floor, The Children's Hospital, Boston, Mass. (Shepley, Rutan and Coolidge, architects.)

are advantages in having a medical man for such a position provided he understands thoroughly that his work is not medical and it is no part of his duty to usurp at any time the function of any member of the medical staff. It *is* his duty to see that the members of the medical staff are punctual and regular in their attendance, and to report to the trustees any dereliction of duty on their part. No member of the

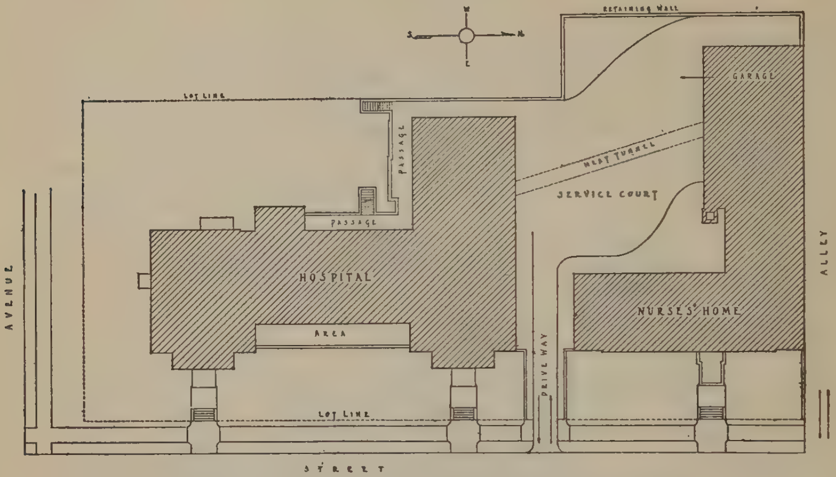


Fig. 167.—Plot plan, Milwaukee Children's Hospital and Nurses Home, Milwaukee, Wis. (Scott and Mayer, architects.)

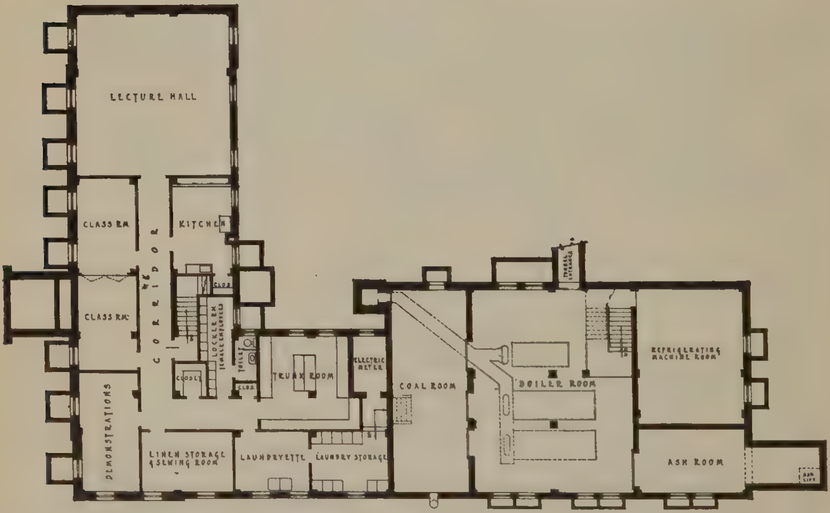


Fig. 168.—Basement, Nurses Home, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

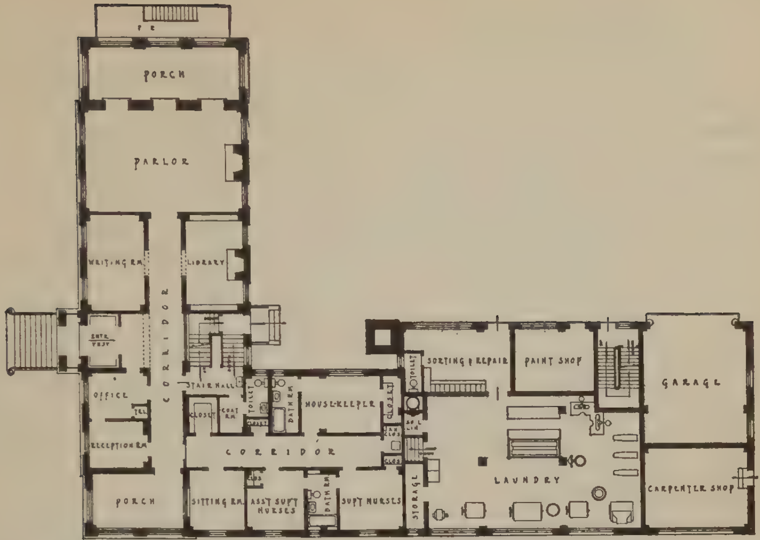


FIG. 169.—First floor, Nurses Home, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

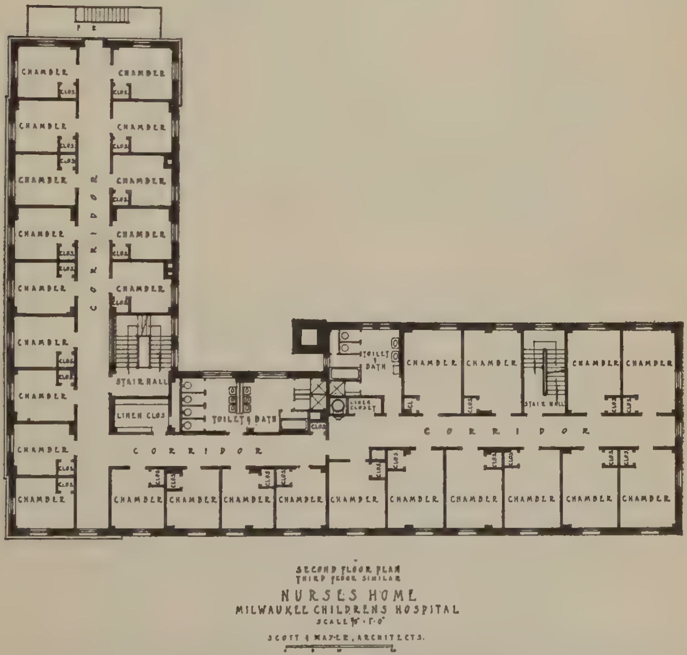


FIG. 170.—Second floor, Nurses Home, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

medical staff should be retained who persistently and flagrantly neglects his service.

Unfortunately the physicians who possess the special qualities and training required by the Superintendent of a hospital and to whom this career has made an effective appeal are very few, and most hospitals must be content with service of a non-medical superintendent. Nor are there enough men superintendents to meet the demand. Many hospitals employ women superintendents, and they have proven thoroughly competent for such work. In the smaller hospitals the woman superintendent may also function as the Director of the School for Nurses.

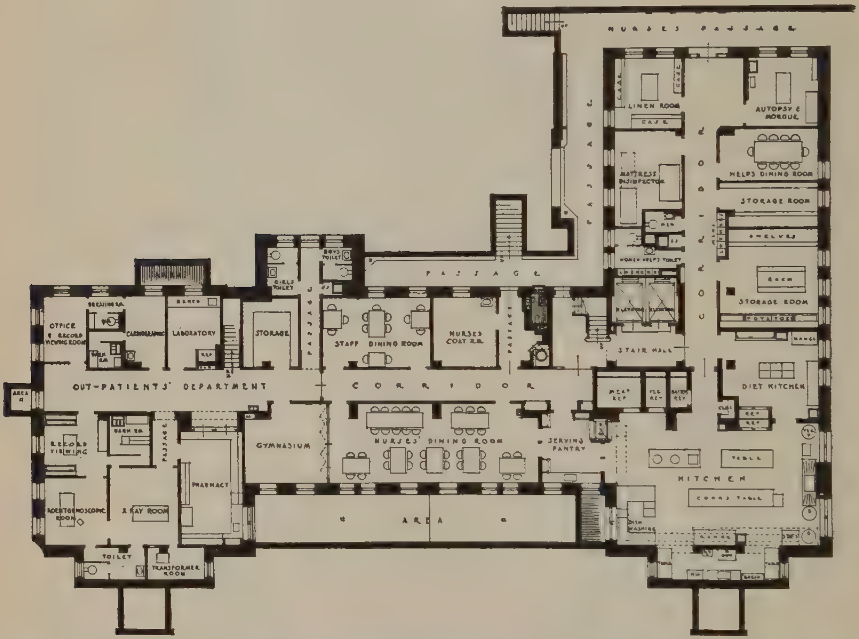


FIG. 171.—Basement, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

A competent superintendent having been selected by the Board of Trustees, he should be given a free hand, with full authority in his domain, and then held responsible for results. Nothing is more inimical to the morale and efficiency of a hopital than dictation to the Superintendent by members of the Board of Directors, a member of the Corporation or others in the selection of employees, purchase of supplies or in any other way. It is not an uncommon occurrence for members of a hospital board or corporation to conceive the idea that employment in the hospital would afford a comfortable home and living for an impecunious relative or friend, and to urge his or her employment with little or no reference to his or her fitness for the job. No Superintendent who is forced to submit to this kind of dictation can be

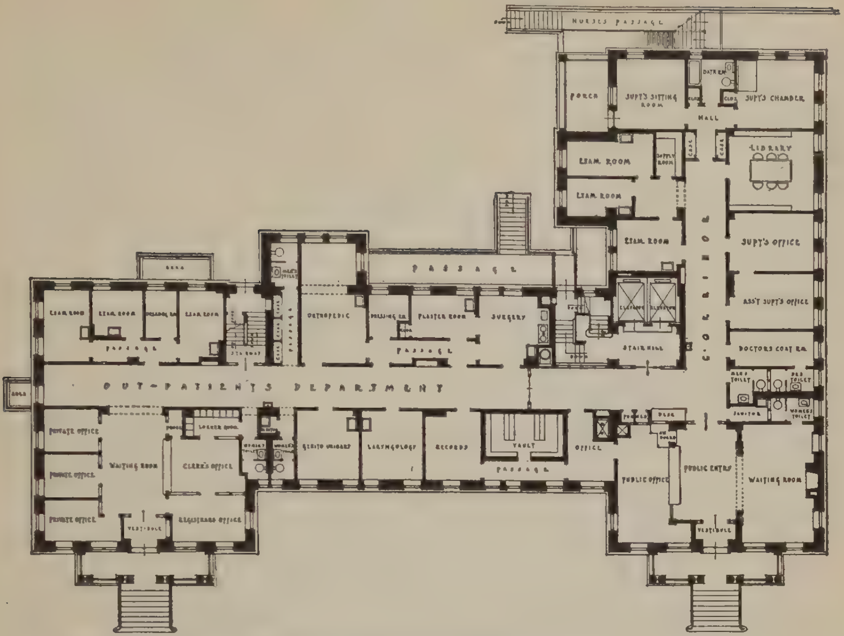


FIG. 172.—First floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

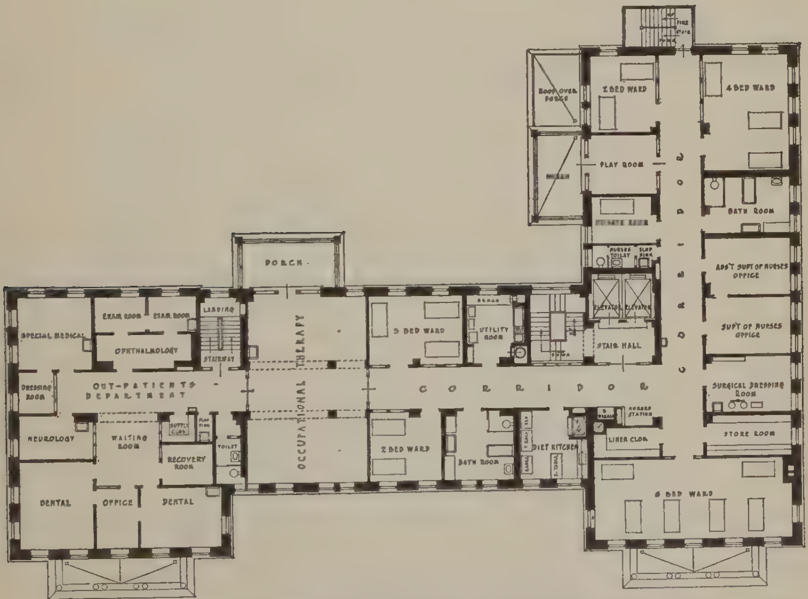


FIG. 173.—Second floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

held responsible for the efficiency of the service. He is the hospital expert, engaged by the Board of Directors, to conduct the hospital for the corporation so as to get the best and most satisfactory results with the least expenditure of money. This he cannot do unless he is given a free hand. On the other hand, he should make frequent reports to the Board of Directors who should meet at least once a quarter and keep in close touch with the work of the institution.

Nursing Service.—The nurses required in a children's hospital may be obtained in either of three ways, or by various combinations of these.

1. The hospital may establish its own training school, securing thereby the service of pupil nurses; (2) It may have a post-graduate school for pediatric nursing, accepting as pupils only nurses who have had training in a general hospital; or (3) the hospital may employ a permanent corps of graduate nurses on salary. The last plan secures much the best service but it is too expensive for most hospitals. Plan 2 is made possible in some parts of the country because of the growing demand for post-graduate training in the nursing of infants and children by those who have been trained in hospitals having no pediatric wards. It should secure a better type of service than Plan 1, because graduate nurses have already obtained a large fund of knowledge and experience which is common to the nursing of the sick of all ages and conditions. The principal difficulty in the way of this plan is the fact that most nurses are unwilling to devote more than a few weeks to such work. Under Plan 1, a school for nurses is organized on the same lines

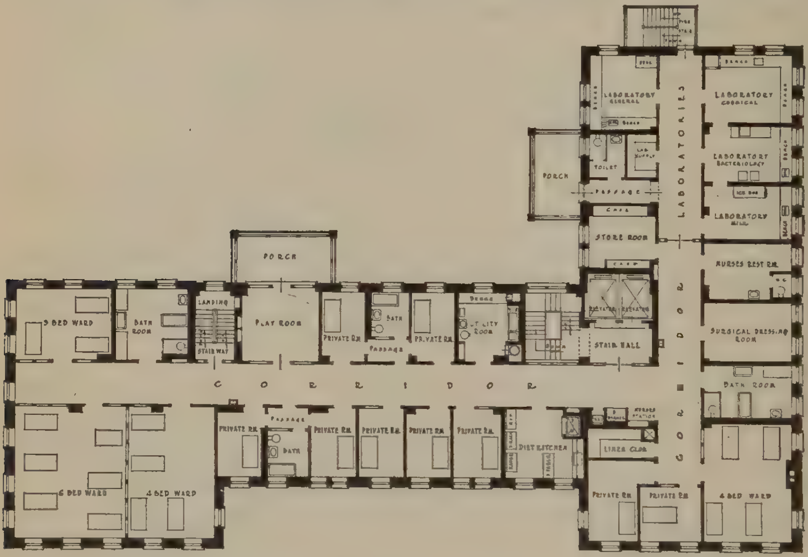


FIG. 174.—Third floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

as those of a similar school in a general hospital, with propædeutic courses in the fundamental branches of anatomy, physiology, bacteriology, etc., and with training at the bedside under careful supervision.

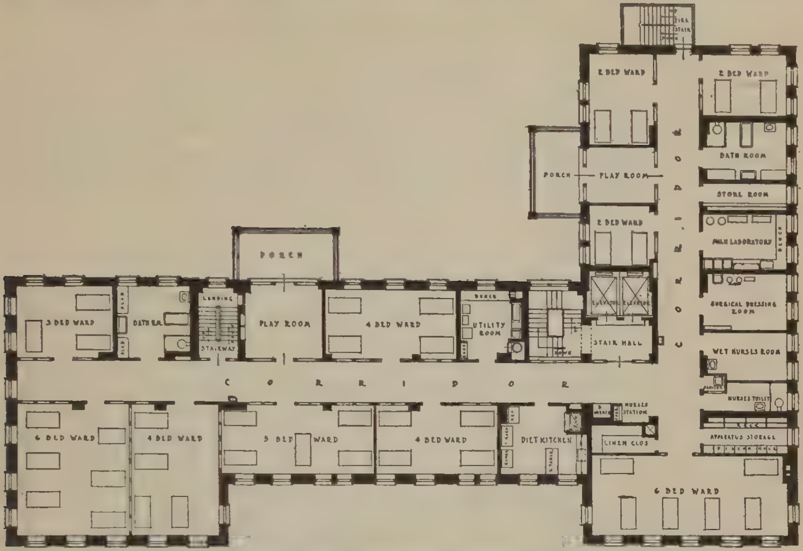


FIG. 175.—Fourth floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

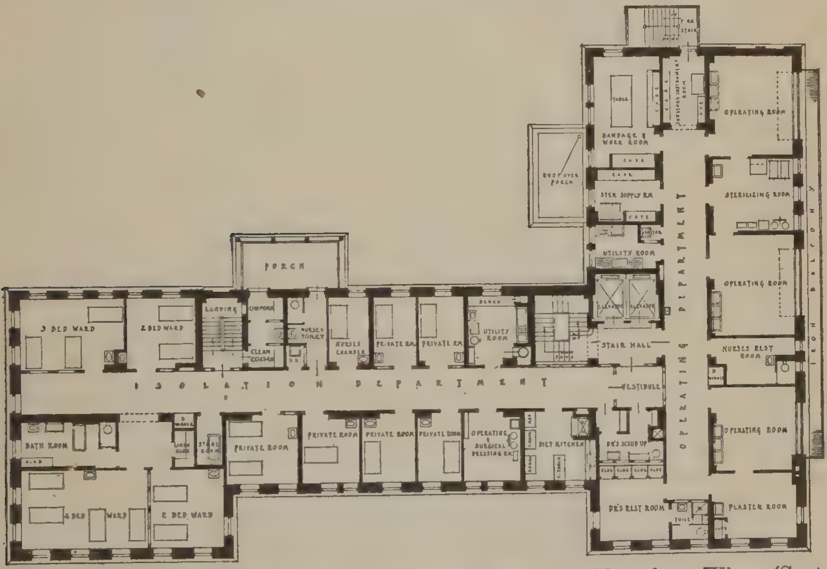


FIG. 176.—Fifth floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

The number of nurses should be such as to provide an average of one pupil nurse for every five or six patients, at all hours excepting at night, when half that number will usually suffice. Eight hours is now generally accepted as the maximum number which a pupil nurse should be on duty each day, and this means three shifts with a full complement of pupil nurses for each of the two day periods and one-half that number for the night shift. One head nurse should have supervision of not more than five or six pupil nurses.

Pupil nurses usually serve without stipend, other than maintenance, the uniforms being supplied by the hospital. Some of the larger hospitals even exact tuition, while, on the other hand, in some institutions each pupil on graduation is given an honorarium of $100, more or less.

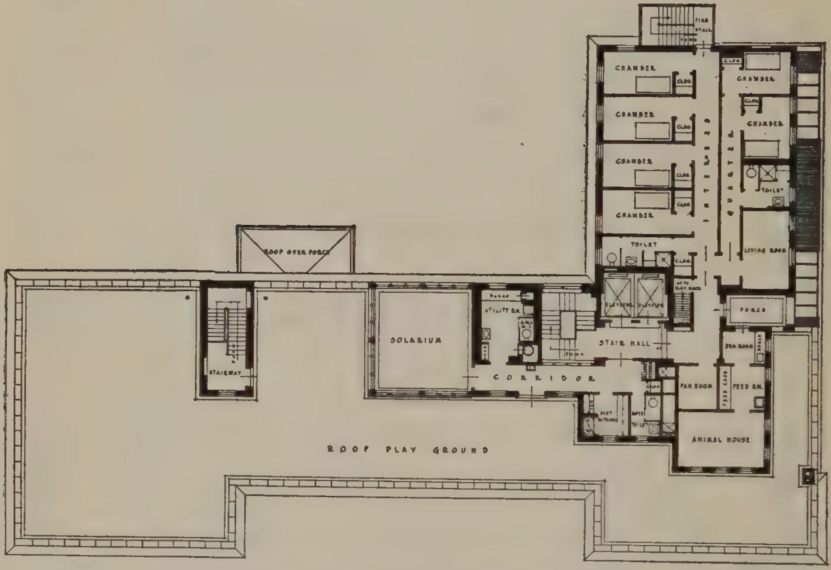


FIG. 177.—Six floor, Milwaukee Children's Hospital, Milwaukee, Wis. (Scott and Mayer, architects.)

A *School* for Nurses must be so conducted as to educate the young women who enter it for the practice of nursing as a profession.

The Function of Instruction in a Children's Hospital.—It is obvious that to secure efficient service for the patients in any hospital the persons having to do with their care must be properly trained in their duties. This applies to the members of the resident staff, the pupil nurses and the social service workers.

The training of the internes is an essential function of the members of the attending staff and they are to be educated not alone for the proper performance of their duties in the hospital, but for a subsequent career as physicians. It is the opportunity which the interneship affords as a training for later practice that constitutes the chief reward for the service they give to the hospital. Fortunately, the kind of training which best fits them for their work in the hospital is practically identical with that which affords the best preparation for independent practice. It consists, for the most part, in a close supervision of the work assigned to them, correction of their mistakes, personal instruction and demonstration in methods of procedure, and rigid insistence on accurate painstaking and thorough performance of those duties which properly belong to them, including accurate and complete clinical histories, recorded as soon as possible after the admission of each patient, careful, thorough physical and laboratory examinations, with full record of the same, and subsequent entry of the daily record of each patient.

One of the most important duties of the attending physician or surgeon is to review at every visit the clinical record of his patients written by the interne, to point out errors and omissions and to instruct him by advice or demonstration when that is necessary. Formal lectures, or quizzes are not essential nor advantageous. The interne has completed in the medical school four years or more of this type of instruction, supplemented by practical work in the laboratory, dispensary and hospital ward, and may be presumed to have a sufficient theoretical foundation for hospital practice. On the other hand, he has seldom had sufficient practice to acquire any high degree of expertness and accuracy in the methods of diagnosis, and these qualities he must acquire by constant practice in the hospital under close supervision. The foregoing statement applies to the interne who comes to the children's hospital direct from the medical college. If the hospital is so fortunate as to procure internes who have already served in a general hospital, or who have been in general practice for some time, there will be found among such men a fair proportion who have acquired a considerable degree of skill in diagnosis. The work of the interne should be so arranged as to give him considerable time to consult the textbooks and standard medical periodicals in connection with his cases, to "read up" on them, and the attenting men whom he is serving should assist in this by supplying the references to the articles most pertinent to each case.

The medical colleges which now require the interne year as a prerequisite for the degree of M.D., and the Boards of Medical Examiners in those states where a year of hospital interneship is required for admission to the examination for licensure have prescribed minimum essentials for a hospital which is to be approved as one in which such interneships may be served. The hospital which does not conform to these regulations will be, hereafter, seriously handicapped in its effort to secure internes, and therefore the hospital officials and the members of the medical staff should be familiar with the regulations prescribed, at least by the medical colleges from whose students they would be most likely to attract internes and by the states in which most of its graduated internes will locate for practice.

The "Minimum Essentials for an Approved Hospital" drafted by the several colleges and State Boards differ widely, and so far no attempt has been made to secure uniformity. The most elaborate

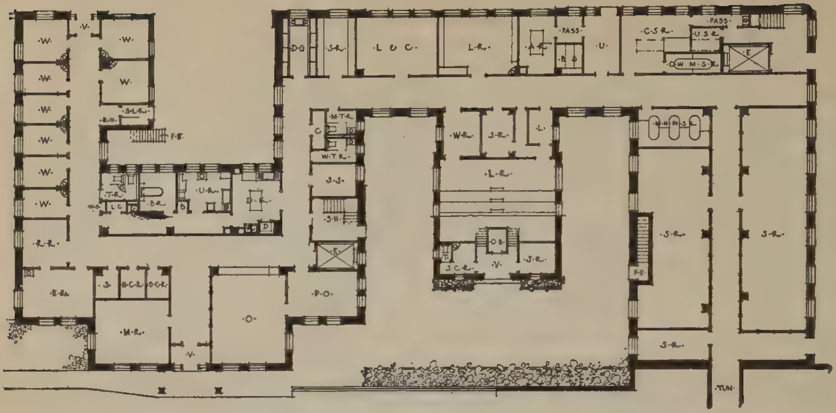


Fig. 178.—Ground floor, St. Louis Children's Hospital, St. Louis, Mo. (Mauran, Russell and Crowell, architects.)

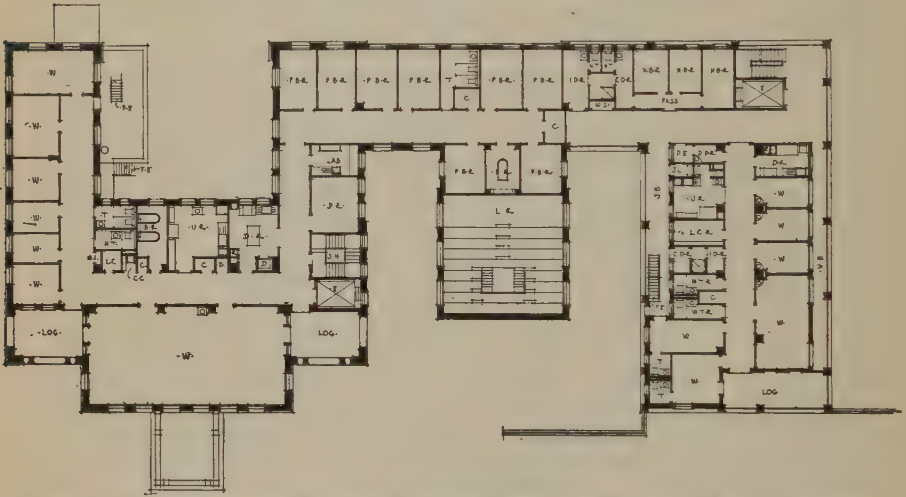


Fig. 179.—Second floor, St. Louis Children's Hospital, St. Louis, Mo. (Mauran, Russell and Crowell, architects.)

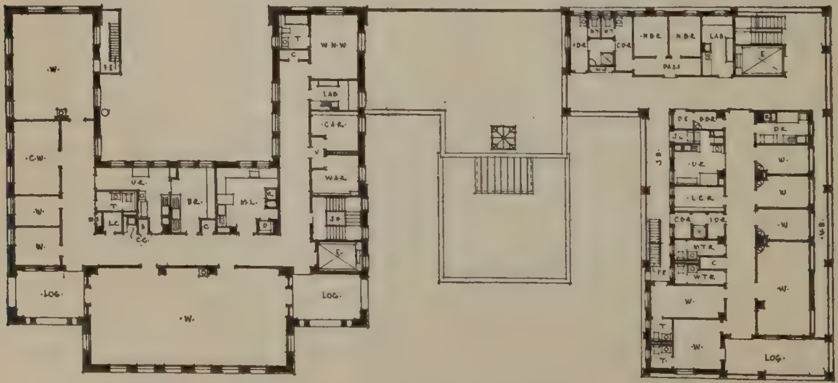


Fig. 180.—Third floor, St. Louis Children's Hospital, St. Louis, Mo. (Mauran, Russell and Crowell, architects.)

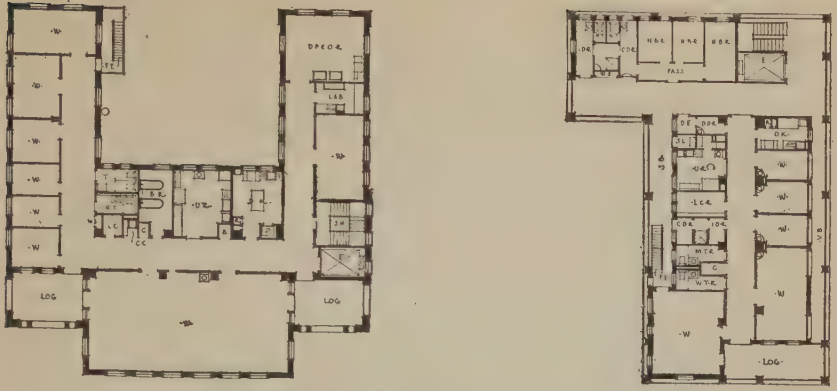


FIG. 181.—Fourth floor, St. Louis Children's Hospital, St. Louis, Mo. (Mauran, Russell and Crowell, architects.)

KEY TO ROOMS

V., vestibule
E., elevator
W., ward
O., office
L., lecturers' room
U., undertakers' room
C., closet
R., refrigerator
D., dumb waiter
B., blanket warmer
S., stretcher and supply room
R.R., reception room
M.R., managers' room
P.O., private office
P.C., porte cochere
E.R., examining room
S.R., storage room
S.S., social ser. room
T.R., toilet room
B.R., bath room
U.R., utility room
D.K., diet kitchen
W.S., wire shaft
L.C., linen closet
C.C., cleaners' closet

T., toilet room
D.R., drug room
S.H., stair hall
R.N., receiving nurse
L.R., linen room
A.R., autopsy room
B.S., body storage
W.R., waiting room
L.R., lecture room
O.B., operators' booth
L.E.C., linen and classes
S.C.R., students' cloak room
W.T.R., women's toilet room
M.T.R., men's toilet room
N.C.R., nurses' cloak room
D.C.R., drs'. cloak room
Pass., passage
S.L.R., soiled linen room
C.S.R., clean sterilizer room
U.S.R., infected sterilizer room
C.W.M.S.R., contag. ward mat. store room
M.H.M.S.R., main hos. mat. store room
P.B.R., private bed rooms
Lab., laboratory
Log., loggia
I.D.R., infected dress. room
C.D.R., clean dress. room
N.B.R., nurses bed room
L.C.R., linen and chart room
D.E., drs'. entrance
D.D.R., drs'. dress. room
S.L., sterilized linens
V.B., visitors' balcony
S.B., service balcony
F.E., fire escape
W.N.W., wet nurse ward
C.A.R., cold air room
W.A.R., warm air room
M.L., milk laboratory
C.W., cubical ward
D.P.E.O.R., dress. plaster and oper. room
D.R., dining room
Int., internes
Res., residents
D.O., directors' office
B.L., bacteriological laboratory
P.L., private laboratory
C.L., chemical laboratory
Cal., calorimetry
A., animal room
D.R., dark room
Bal., balance room
Tun., tunnel to Barnes Surg. Ward
N.T., nurses' toilet room
L.E.R.R., library and recreation room

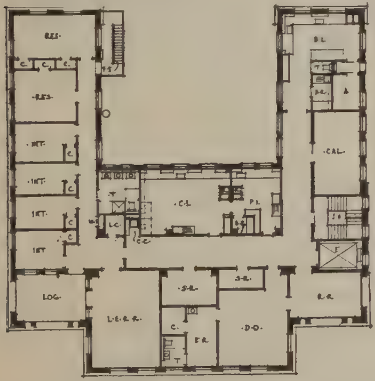


FIG. 182.—Fifth floor, St. Louis Children's Hospital, St. Louis, Mo. (Mauran, Russell and Crowell, architects.)

and detailed regulations are those of the Pennsylvania State Board of Medical Examiners which go so far as to specify in minute detail, the laboratory equipment which a hospital must possess, with corresponding minuteness in the other features of hospital activity.

Perhaps the most brief and simple draft which has appeared is that of one of the medical schools which is here presented:

MINIMUM ESSENTIAL SERVICE OF INTERNES FOR AN APPROVED HOSPITAL

Equipment:

Beds.—At least 60.

Patients to be medical (daily average of 10 or more), surgical (daily average of 10 or more) and, if possible, obstetric.

Laboratory and its equipment—adequate and up-to-date.

X-ray apparatus—adequate for all necessary purposes.

If possible, a library—accessible; supplied with necessary books of reference and important current medical periodicals.

Food—wholesome and sufficient.

Quarters for internes—clean, comfortable and conveniently located.

Filing cases or room for clinical histories.

Interne Service:

Length—at least one year.

Type—mixed, rotation, or single department; if the latter, with privilege of extension to an opposite service, e.g., the medical to surgical or *vice versa.*

Contract—to be written or printed and signed by interne and hospital authorities.

Senior and junior internes—when possible, the arrangement should be made for a senior and a junior interne on the same service.

Rules and regulations—copy printed or mimeographed for each interne.

Medical Staff:

An organized, responsible staff of physicians of unquestioned professional character, competent, each in his special line, and who agrees to supervise closely and direct the work of the internes, one or more of the staff to serve as local supervisors of internes and to make reports to this college.

Pathologist—staff to include a competent, full or part time pathologist who shall supervise and direct laboratory work of internes.

Attendance of staff—one or more members of each department to attend daily; each member at least twice weekly when on active duty.

Work of Internes:

Type—such as properly belongs to internes, not that of orderlies, nurses, et al.

Amount—no interne to be assigned more patients then he can care for adequately.

Hours—routine work to occupy not more than 8 or 10 hours daily.

History writing—thorough clinical histories, promptly written, to be insisted upon from each interne. Attending men to review and insure correctness of same. Subsequent entries of operations, laboratory findings, *x*-ray findings, etc., and progress and outcome of the case to be promptly initialed. Routine laboratory work to be promptly and accurately done, and checked by the pathologist.

Operations—an interne assisting at surgical operations should be assigned such duties and should be so placed that he can see the operation (unless he is serving as anesthetist).

FIG. 183.—St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

Meetings of the Medical Staff and Internes.—Meetings of the medical staff and internes should be held at least once each quarter.

Between this simple, brief statement of minimum essentials and the elaborate prescription of the Pennsylvania State Board, the requirements of other medical colleges and boards present varying degrees of detail.

Altogether the most important item in the function of education of the interne is the character, the ability and the spirit of the physicians on the attending staff. If they are possessed of a warm, sympathetic interest in the internes, and a willingness to give the necessary time and attention to their supervision and training, good results are bound to be realized, even though other conditions are not ideal.

The Training of the Nurses.—Just as the internes enter the hospital and give their services, because of the opportunity it affords for their training for independent practice, likewise the pupil nurses are there to be trained, not only for their duties in the hospital, but to secure an education for a career as a professional nurse. They enter the hospital, therefore, as pupils of the School for Nurses, the Director of which is usually the Superintendent of Nurses in the hospital, the faculty of the school being composed, in part, of members of the medical staff of the hospital, who give instruction in some of the

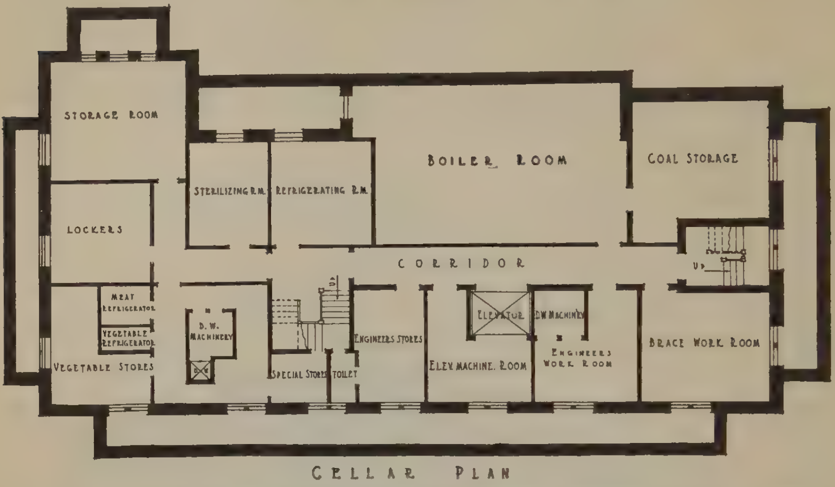


FIG. 184.—St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

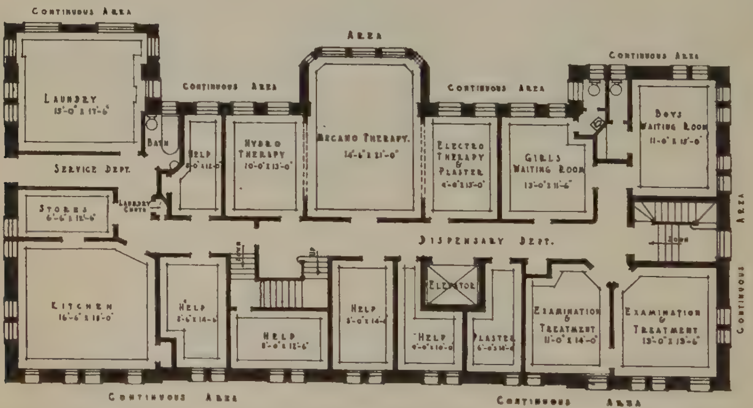


FIG. 185.—Basement plan, St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

fundamental medical branches—anatomy, physiology, bacteriology and the like—and in larger part, of members of the nursing corps who give instruction in the principles of nursing and supervise the work of the pupil nurses in the hospital.

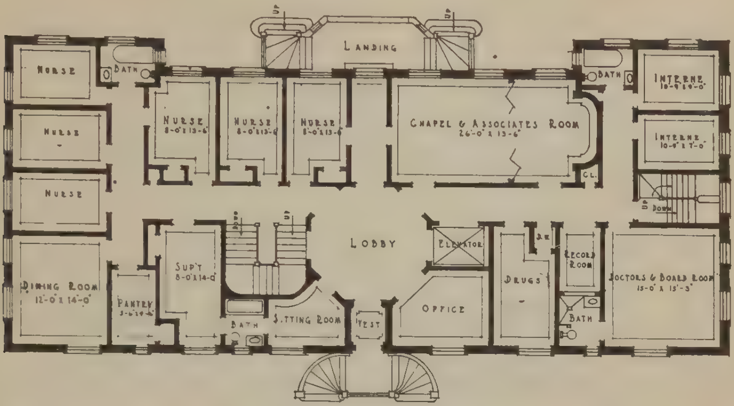


FIG. 186.—First floor, St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

Such training schools in the smaller hospitals have too often been "schools" only in name, while in reality they have been but mean devices for securing cheap help. Long hours of work, usually 12 daily, have been exacted, a good deal of the time being taken up with menial work of various sorts which does not rightly belong to the nurse.

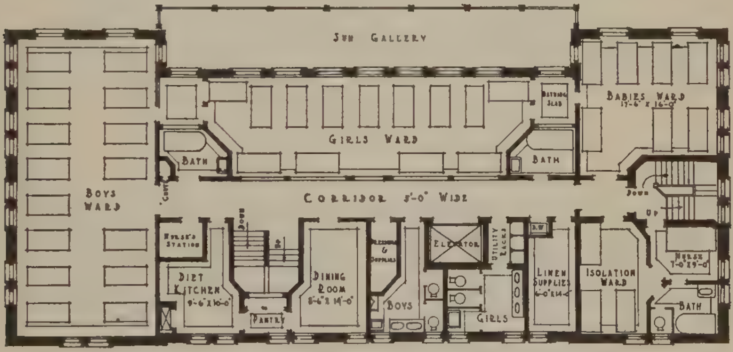


FIG. 187.—Second floor, St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

No pupil nurse should be assigned work for more than eight hours for the day, and the eight hour day is becoming generally recognized as the proper arrangement for the pupil nurse.

The social service worker is a most useful aid to the physician in the care of patients in the Out-patient Department, and in the follow-up work in connection with hospital patients after they have been discharged from the institution. Up to the present time, social service workers have been trained, for the most part, by actual work in this field, with little formal instruction in the theoretical phases of sociology. Each hospital should have a director of social service, part of whose function it is to organize and conduct a scheme of training for her subordinates. Doubtless in time there will be organized a systematic course of instruction for such workers in the hospital service field, the first year consisting of instruction in the department of sociology of a college or university, to be followed by one or two years of practical experience, under supervision, in dispensary and hospital.

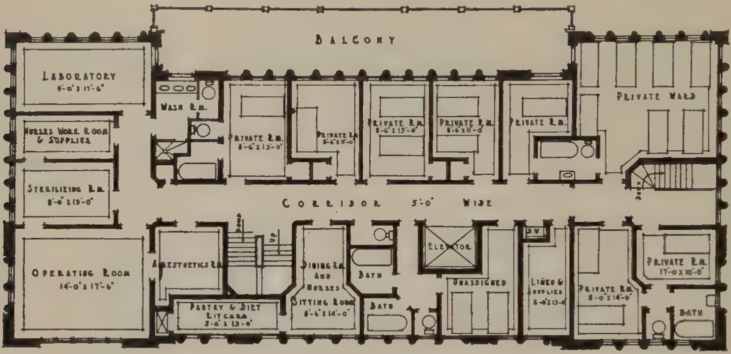


FIG. 188.—Third floor, St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

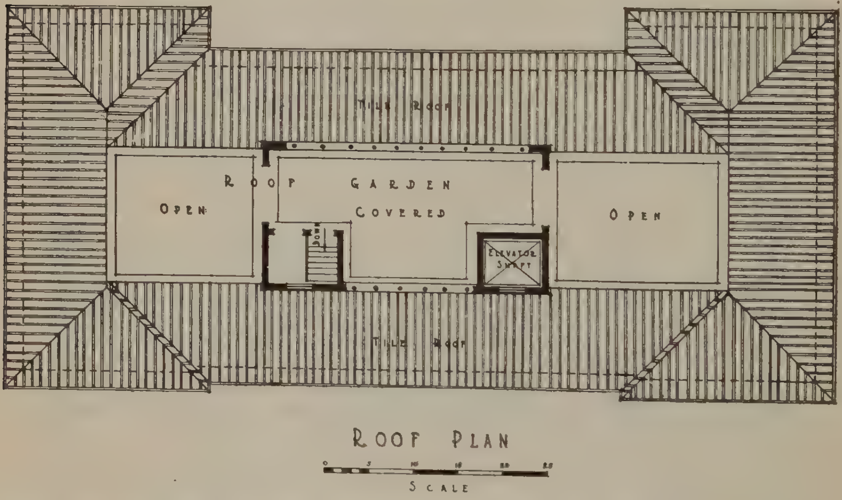


FIG. 189.—St. Giles Hospital for Crippled Children, Brooklyn, N. Y. (Ludlow and Peabody, architects.)

Continuation Courses in Pediatrics for Practitioners.—No children's hospital is realizing its full possibilities for usefulness unless it offers opportunity for the instruction of general practitioners. The advance in our knowledge of the diseases of infancy and childhood in the last few years has been so rapid that very few family doctors have been able to keep abreast of it. Textbooks and journals do not alone suffice. The physician engaged in general practice needs to get away at intervals from the distractions of his daily routine and to devote himself intensively for a few weeks to the study of medicine, to refresh his knowledge of the old and to acquire familiarity with the newer facts and methods. Nowhere can he do this to such advantage as in a well-equipped hospital with an organized, earnest staff of capable specialists. Every children's hospital of sufficient size—40 beds or more—should offer opportunities for continuation study of pediatrics by the practitioners in its vicinity. Some members of the staff should offer courses on the anatomy and physiology of infants and children, illustrated by anatomical specimens (dissected parts, cross-sections and the like), by charts, models and drawings. Embryology is an important subject and opportunity should be given for the study of gross specimens and serial sections of embryos at various stages of development. Courses in biologic chemistry, bacteriology and pathology should be offered by various members of the staff, conducted, in so far as possible, in the laboratories, where the physician comes in first hand contact with the materials to be studied. The newer methods of laboratory diagnosis, the newer instruments of refined diagnosis and the methods of treatment, especially in the line of infant feeding, are all important, and opportunity to acquire knowledge of these matters, as well as some facility in their use, is eagerly sought by many physicians.

The Education of Mothers.—The instruction of mothers and others in the care, especially of infants, is a field of great usefulness which no children's hospital should neglect. In connection with the Out-patient Department, there should be maintained an Infant Welfare Department, with a sufficient staff of competent physicians, nurses and social service workers devoted to the interests of the infants of the less well-to-do families of the community who are not sick and who can be kept well if they are given proper feeding and care. This is *preventive medicine* of the *most essential* and useful type.

Hospital Financing.—Among the important functions of the Board of Directors is to (1) secure funds for the maintenance of the hospital, (2) to see to it that these funds are expended wisely and economically, so as to procure the largest possible results in service for the money expended, and finally, (3) to insist that the methods of book-keeping and accounting shall be such as will enable the Board to ascertain at any time the exact financial status of the institution.

1. The sources of income for the maintenance of the hospital depend upon the class to which it belongs. A purely public hospital for children, erected by the community (city, county or district), is supported by funds obtained through taxation and appropriated

to its use by the City Council, Board of Supervisors of the county or other similar governing body. A purely private hospital, conducted for profit, derives its funds from the fees paid by the patients. Few hospitals for children belong to either of these groups. For the most part they are semi-public institutions, receiving in a few instances charity patients only, but as a rule both pay and free patients. The pay patients can be conveniently grouped into (*a*) those who pay the full hospital rates, a sum, properly enough, considerably in excess of the actual cost of the service rendered them; and (*b*) those who pay such sums as they are able, but which fall short of the full rates.

If the patients in the hospital are largely of the full-pay class, the surplus obtained from this source may be sufficient to defray the whole expense of the hospital, including the care of the small proportion of free and part-pay patients who are admitted. This is very rarely the case, particularly in a hospital for infants and children, and so there must be other sources of income.

These may be (1) endowment funds from individuals, by gift or bequest, or from churches, societies or other organizations. Under the terms of such a gift, the income may be available for general purposes of the hospital, or, as is much more commonly the case, such an endowment is given for a specific purpose, usually the maintenance of a bed, room or ward; (2) pledges of money for the support of the hospital may be given by individuals or organizations to be paid annually; (3) money may be raised by entertainments, bazaars and the like, by personal solicitation of the officers or other friends of the hospital, or on hospital "tag day," when all the citizens are asked to give such sums as they feel inclined to give, receiving in return tags showing that they have contributed.

From the viewpoint of the hospital corporation and its Board of Directors, an original endowment sufficient to yield an income that will cover the full cost of maintenance is very comforting and satisfactory, but very few children's hospitals have been so endowed. On the other hand, there are advantages in the financial status of most hospital organizations which make it necessary to seek sources of income each year. The hospital, to be of largest service to the community, needs the active interest of as many persons as possible, and no bond of interest is so effective as that created by a contribution to the support of the institution.

In so far as possible, the burden of actually raising funds for maintenance of the hospital should be assumed by other organizations rather than by its Board of Directors and the officials. Their task is to so conduct the institution as to secure the largest possible results from the funds available and the more completely their time and energies can be devoted to this work, the more they are relieved of the job of raising money or worry over a possible deficit, the better.

Patients consigned to the hospital who are properly charges on the community at large—the pauper group—should be paid for by public funds appropriated to the hospital by the City Council, the Board of County Commissioners or whatever body is in control of such funds. An annual appropriation to the hospital for this purpose should be made, approximating in amount the cost of the service which the hospital is expected to render to this class of patients. This appropriation should be available at the beginning of each fiscal year, an account to be rendered by the hospital at the end of the year, when a balance is struck and the deficit made good to the hospital of surplus returned to the public treasury as the case may be.

Churches, benevolent societies, industrial concerns, labor organizations or individuals should be induced to give endowments for the maintenance of free beds or to pledge stated sums each year to the support of the hospital in return for which they are given the right to send sick children to the hospital, at any time in the case of an endowed bed, when it is unoccupied by a patient previously sent by them, or, if the donor gives a certain amount annually, for such number of days as will equal, in cost of maintenance, the sum given the donor.

The endowment of beds, rooms or wards is as a rule for such sums of money as will yield an income, at the usual rate of interest, sufficient to pay for the anticipated cost of maintenance forever, and such beds have been generally designated as "*Free beds in Perpetuity.*" The Board of Directors should exercise caution in accepting such endowments and contracting to maintain a bed or beds, as "Free beds in Perpetuity," unless either the endowment is so large as to absolutely insure an income sufficient to pay the cost of bed, room or ward, however such cost may increase in the future, or a reservation is made in the contract providing that should the cost of maintenance at any time come to be greater than the income from the endowment, the hospital may have the right to use the beds, in part, for pay patients. Few endowments have been so guarded in the past, and in recent years there have been many instances in which hospitals, faced with an enormous increase in the cost of conducting the hospital, have diverted these "Free beds in Perpetuity" to the use of pay patients, without the knowledge and consent of the donors. Such an action is plainly a violation of the original contract, although the continued use of these endowed beds at the doubled cost would have resulted in the financial embarrassment of the hospital. The proper course in such a contingency is to present the facts to the original donor, or to his heirs, and to ask that the endowment be increased by such an amount as will support the beds under the changed conditions. In the great majority of cases the response to this request will be prompt and satisfactory.

By whatever means and from whatever source the income of the hospital is obtained, it is the duty of the Board of Directors to see that the expenditures of the hospital are kept within its income each year. A shortage may be anticipated when the budget for the coming year is drawn up, but contributions should at once be secured to make up this shortage so that there shall be no deficit at the end of the year.

Nothing so commends a hospital or other charitable institution to the confidence and good-will of prospective donors, as evidence of good, business-like management of its finances.

Hospital Expenditures.—The insurance of economy in the financial management of the hospital devolves primarily on the Superintendent. In choosing the person who is to occupy this important position, his (or her) possession of a thorough business training and of those qualities which are essential to this end should be a first consideration.

He must be able to select employees who will render faithful, efficient and full-time service for a reasonable wage, and to know that they are daily rendering full service; to purchase supplies, of all sorts, of satisfactory quality, at the lowest market price; to eliminate waste in the use of hospital materials such as food, fuel, linen, surgical dressings, and other medical supplies, a difficult task when so many persons, physicians, nurses, cooks and other employes are concerned in the use of these articles. He must command the confidence and be able to secure the hearty, sympathetic coöperation of all persons who work in the institution, in the effort to keep down the expenditures of the hospital to the lowest point consistent with efficient service. It is his duty to see that the persons able to pay for hospital care are not admitted to the free beds, but required to pay such sums as they are able to pay. In this he should have the coöperation of the medical staff. He should make report to the Board of Directors at frequent intervals—at least quarterly—setting forth clearly the financial transactions and status of the institution.

Hospital Accounting.—The methods of accounting and bookkeeping in a hospital are essentially the same as for other business enterprises of similar character, for example, of a hotel. They should be sufficiently comprehensive and detailed to convey to the Board of Directors at any time an accurate knowledge of the pecuniary operations of the institution and of its financial status. On the other hand, the scheme should not be so complicated and detailed as to require many unnecessary entries and unreasonable labor and expense.

A number of systems of accounting and book-keeping for such enterprises have been devised and placed on the market in recent years. It is not necessary or feasible to present such plans in this article. Information in regard to these various systems of hospital accounting can now be obtained at the Library and Service Bureau of the American Conference on Hospital Service, established in 1920, and located in Chicago. This Bureau is now prepared to furnish information in regard to all phases of hospital organization, maintenance and activity, as indicated by subjoined tabulation of items.

OUTLINE OF MATERIAL BEING COLLECTED
BY THE
HOSPITAL LIBRARY AND SERVICE BUREAU

of The American Conference on Hospital Service
22 East Ontario St., Chicago

I. The Hospital Field

- I. The hospital field.
  - Methods of determination of needs of
    - Hospital
    - Health center
    - Dispensary
    - Sanatorium
    - Service.
  - Community surveys, methods of community organization and preliminary planning.
  - Financing........
    - Methods of estimating capital funds for construction and maintenance.
    - Finance committee organization.
    - Securing funds for buildings, endowment, current expenses, etc.
    - Aid from public funds—data to be compiled from state laws.
    - Publicity methods employed in financing.
    - Community chests and federated charities.
    - Educational campaigns and "drives."
    - Free beds and wards.
  - Types of hospitals
    - Classed by control
      - Public......
        - Regional and sectional.
        - Town.
        - Municipal
        - County.
        - State.
        - Federal.
      - Incorporated
        - For profit.
        - For profit, but also offering free service.
        - Not for profit.
      - Proprietary
        - Personal ownership.
        - Group or mutual ownership.
        - Corporation.
        - Association.
        - Denomination.
    - Classed by service rendered.
      - General.....
      - Special......
        - Nervous and mental.
        - Isolation.
        - Tuberculosis.
        - Convalescent.
        - Children's.
        - Orthopedic.
        - Maternity.
        - Surgical.
        - Eye.
        - Ear, nose and throat.
        - Skin and cancer.
        - Medical.
        - Diagnostic.
        - Drug addiction.

II. Construction of Hospitals

- Location of hospitals (in relation to
  - Traffic.
  - Accessibility.
  - Noise.
  - Purity of air.
  - Light.
  - Sanitation.
  - Future growth.

- II. Construction; hospitals, dispensaries, sanatoriums.
  - Floor plan files.
    - Hospital as a whole.
    - Special departments.
      - Administration.
      - Kitchens.
      - Wards.
      - Operating rooms.
      - Dispensaries.
      - Nurses' homes.
      - Service buildings.
      - Recreation.
      - Heating, lighting and ventilating systems.
      - Laboratories
        - Pathological.
        - *X*-ray.
        - Clinical.
        - Serological.
        - Metabolic.
        - Dietetic.
        - Departmental.
  - Grounds
    - Layout.
    - Index of landscape architects.
    - In relation to recreation of patients, nurses,釘internes, etc.
  - Follow-up comment on plans after a year of operation.
  - Materials
    - General description and serviceability.
    - Comparative costs, etc.
  - Index of architects, consultants, and builders.
  - Costs of buildings
    - Records of building costs as far as obtainable.
  - Equipment
    - Lists of equipment used in individual hospitals, dispensaries, and special clinics.
    - Costs of equipment placed in individual hospitals.
      - Hospitals.
      - Departments.
      - Follow-up comments on equipment after one year of use.

III. Operation of Hospitals

- III. Operation
  - Development of general internal organization.
    - Diagrams of organization.
    - Literature on organization, constitution and by-laws in use.
  - Affiliation with
    - Medical schools.
    - Church.
    - Industry.
    - Others.
  - Community relations with
    - City, town, and county.
    - Local relief-giving organizations.
    - Public or legal supervision of illness and health.
  - General relations
    - With national, state, health, hospital, professional, and departmental activities and organizations.
  - Staff
    - Qualifications.
    - Organization.
    - Responsibilities.
    - Work.
    - Staff meetings.
    - Professional records
      - Policies.
      - Principles.
      - Systems...
        - Equipment costs.
        - Maintenance costs.
  - Nursing
    - Scholarships.
    - Schools of nursing.
    - Graduate supervision.
    - Graduate for private duty.
    - Graduate for floor duty.
    - Trained attendant.
    - Practical attendant.
    - Orderly.
  - Laboratories
    - Pathological.
    - *X*-ray.
    - Clinical.
    - Serological.
    - Departmental.
    - Metabolic.
    - Dietetic.
      - Organization.
      - Plans and space.
      - Equipment.
      - Work and relation to other departments.
      - Charges for work.
      - Policies as to free work.
  - Purchasing
    - Equipment
    - Supplies
    - Special
      - Methods and policies in use.
      - Sources of supply.
  - Mechanical
    - Engineering and all mechanical departments.
      - Policies and plans in use for securing and supervising.
  - Dispensary (when a department)
    - General organization.
    - Staff organization.
    - Community relations.
    - Social work.
    - Policies as to fees.
    - Follow-up work.
  - Social work
    - Organization of department.
    - Policies and work.
    - Relations to
      - Hospital executive.
      - Staff.
      - Schools of nursing.
      - Community agencies.
  - Accounting
    - General principles.
    - Policies in use.
    - Systems.
  - Charges for service
    - General principles.
    - Policies in use.
    - Record of schedules used by hospitals of different sizes, classes, etc.
    - Provision for free service.

IV. Training of Hospital Personnel

IV. Training of hospital personnel	Administrators. Nurses. Laboratory and *x*-ray technicians. Pathologists. Dietitians. Anesthetists. Social workers. Internes. Occupational therapists. Physio-therapists.	Schools. Courses. Methods. Qualifications. Scholarships.

V. Organized Activities Bearing on the Hospital Field

- V. Organized activities bearing on the hospital field.
  - Direct
    - General hospital associations.
      - U. S. and Canada.
      - Foreign.
      - State.
      - Local.
    - Professional associations . .
      - Medical.
      - Surgical nursing, dietetic, social service, etc.
    - Departmental associations
      - Social service.
      - Dietetic.
      - Nursing.
      - Laboratory
        - Pathological.
        - *X*-ray.
        - Clinical.
        - Serological.
        - Metabolic.
        - Dietetic.
        - Departmental.
  - Related
    - Public health. . . . .
      - Sanitation.
      - Mental hygiene.
      - Social hygiene.
      - Tuberculosis.
      - Housing.
      - Child welfare.
      - Nutrition clinics.
      - Health centers.
      - Venereal disease clinics.
    -
      - Public health.
      - Schools of nursing.
      - Home instruction in care of the sick.
      - Industrial.
      - Military.
    - Government. . . . .
      - Army.
      - Navy.
      - Public health service.
      - Other departments producing material of value to hospitals.

VI. Associated Information

- VI. Associated information
  - Vital statistics.
  - Insurance reports
    - Life.
    - Maternity
    - Sickness.
    - Accident.
    - Industrial.
    - Fire.
    - Tornado.
  - Compensations or subsidies.
    - Industrial
      - State
      - Direct
        - Policies and methods in use.
    - From other insurance.
    - From city, county, or state.
  - Legal
    - Decisions.
    - State and Federal laws and municipal ordinances affecting hospitals.
    - Pending legislation.
    - Proposed laws.

VII. Hospital Literature

- VII. Hospital literature
  - Libraries.
  - Books, publishers, and authors
    - Subject and author's index.
  - Periodicals.
  - Reports. . . .
    - Federal.
    - State.
    - Municipal.
    - Hospital.
    - Health departments.
    - Surveys.
    - Medical and health organizations.
    - Schools.
    - Conferences.
  - Hospital statistics.

Location—Hospital Site—Planning.—The Superintendent and the Medical Staff, having been agreed upon, and their expert advice being available, the site of the hospital is to be selected and the plan of the building determined. In the decision of these questions the Board of Trustees should seek the advice of those having expert knowledge, including the Superintendent, members of the Medical Staff and a hospital architect. Many of the older hospitals were designed by architects who had had no experience and who had given little study to the needs and purposes of hospitals. An inevitable result was the sacrificing of these needs to architectural effect. Fortunately the large and increasing demand for hospitals has led a considerable number of architects to give special attention to this type of work, and the services of a designer who is an acknowledged expert in hospital architecture are now available everywhere in the United States.

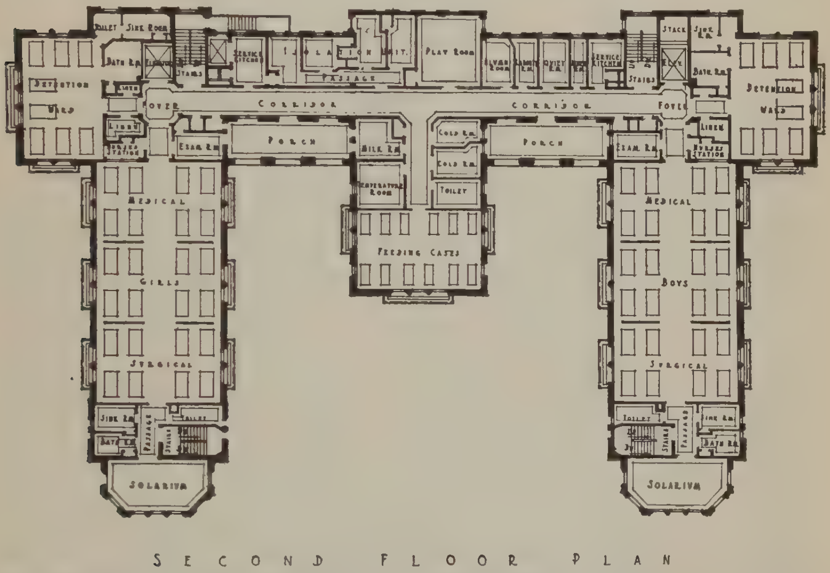


Fig. 190.—New Cumberland Street Hospital, New York City. (Ludlow and Peabody, architects.)

It seems of particular importance to state that the planning of a hospital should not be begun until a generally complete also detailed program of the building plans is set up. This program must regard the future operation in its smallest and largest elements, and can only be set up by the medical direction which will have charge of the institution.

The program and building plan must accord with operation and it is difficult, almost impossible, certainly only with many complications, that operation can be adapted to an unsuitable building.

Building plan and operation are more interdependent in a hospital than in any other kind of a building.

Inasmuch as the hospital organization will not always be found to be trained or experienced to readily prepare such a program, it is the custom to collect information by junketing trips of inspection of existing institutions.

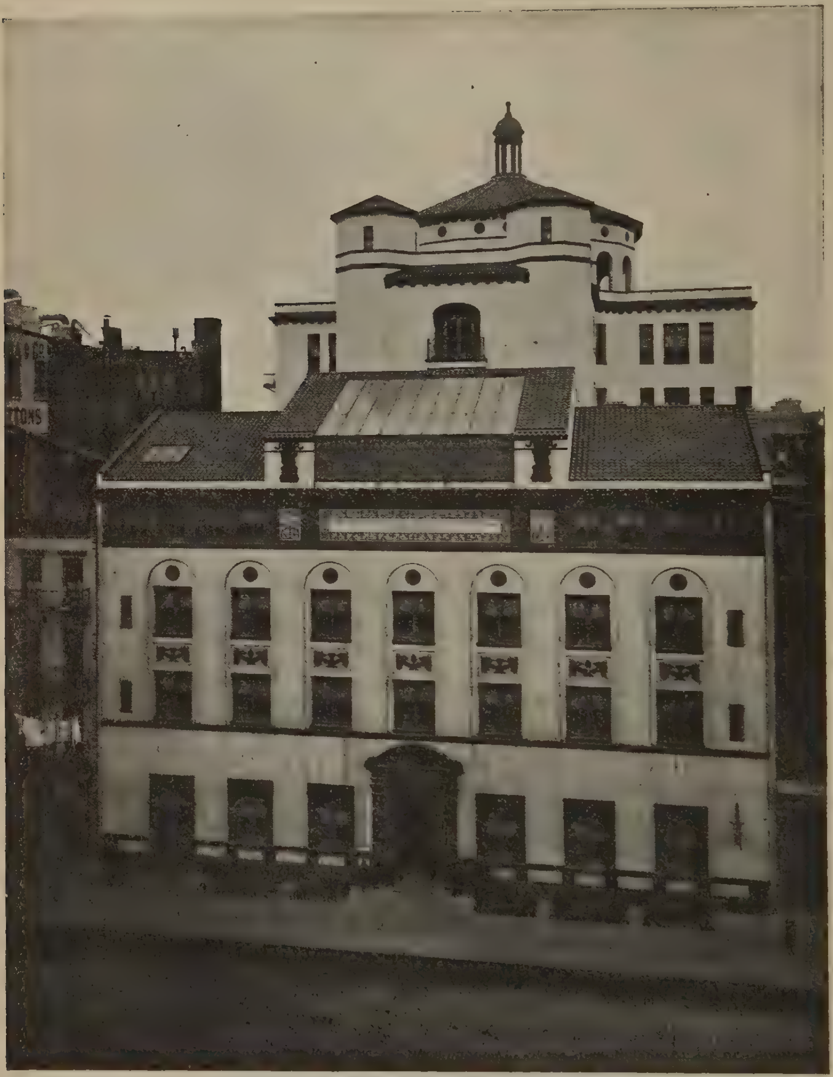


FIG. 191.—New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

The value of such trips cannot be deprecated but it is doubtful if the views and impressions obtained in so short a time are sufficient. at least not without careful study which is not generally obtained.

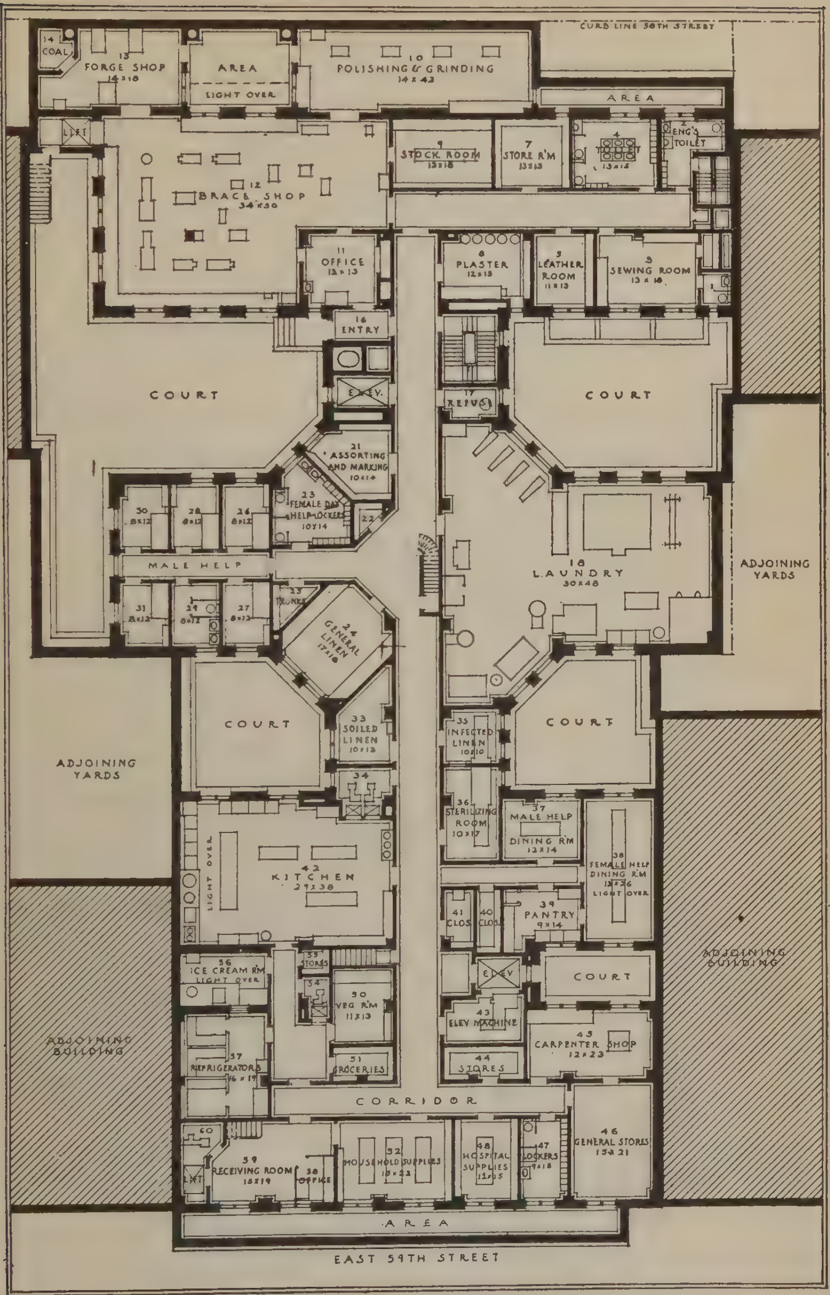


Fig. 192.—Basement, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

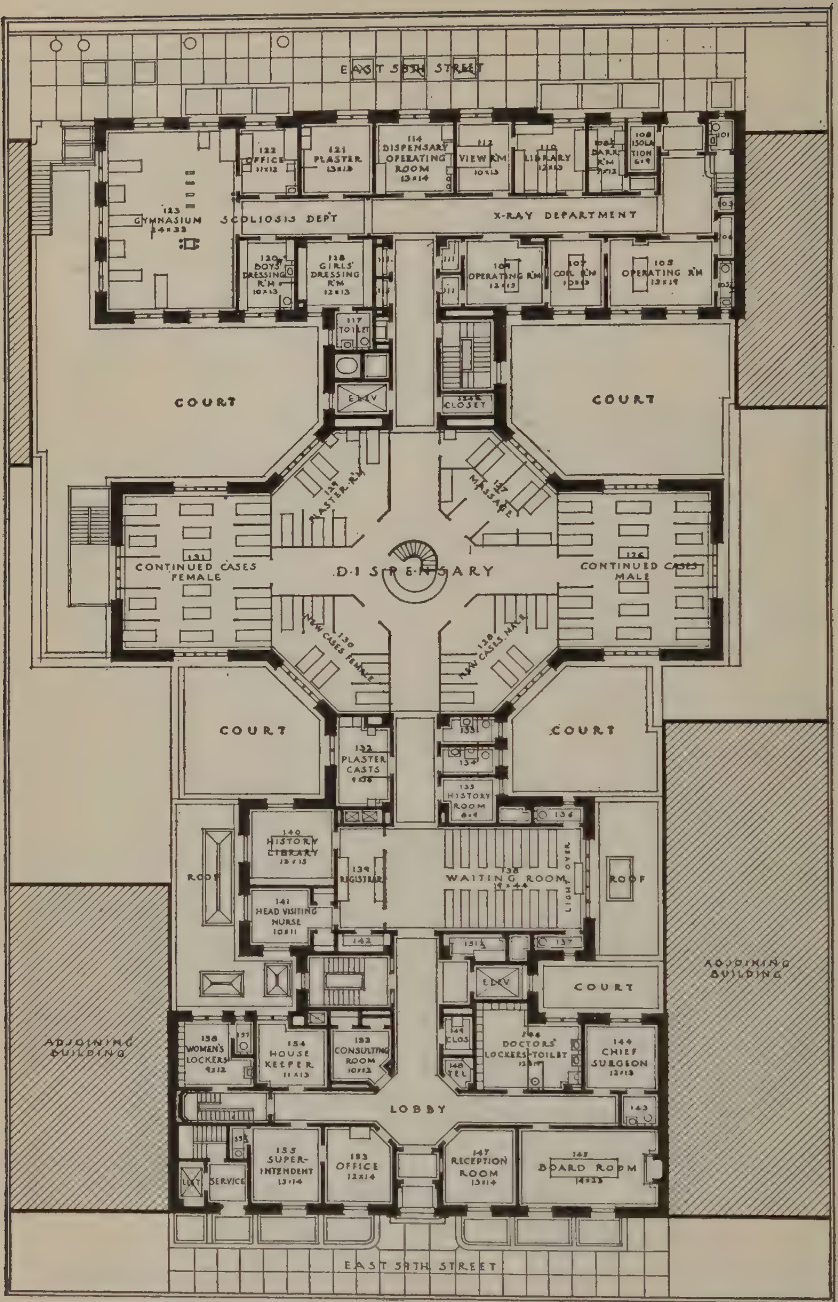


FIG. 193.—First floor, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

Personal experience and long research made without regard to the particular building in hand seem necessary.

The popular method to entrust the planning and building of an institution to a more or less inexperienced committee of laymen usually results in a building difficult and inconvenient of operation. Such committees may be a necessary evil; if so, they should accept the advice of experts.

It is also a widespread error that every physician can develop a particularly important activity as a member of such a committee. On such, only those physicians are suitable who have had a wide experience in hygienic and institutional matters. The results will be the most successful if the building committee will consider and approve the recommendations of the physician experienced in such matters and the experienced architect.

After the program of the proposed hospital has been framed the experienced physician, the expert architect and the Superintendent must work together to develop the general building plan and all its details in coördination with the plan of operation.

If the hospital is to be large the appointment of the operating engineer early in the development of the building is valuable and important; obviously time is required to learn all of the intricacies of the mehanical equipment of a large modern hospital.

The program should indicate the limiting lines and it is the architect's problem to find their architectural expression.

The selection of an architect for a hospital is a difficult one. Innumerable and repeated experiences in the use of materials, in hospitals, arrangements, details and generalities should be the deciding factor in making a choice and it should be remembered that not every architect is or can be a good or an expert hospital architect.

It is necessary to entrust the work to a specially expert architect to insure success, one who possesess the requisite knowledge of the many important questions which will arise and who has obtained this knowledge by extensive experience.

It is not enough that the architect has informed himself to some extent, possibly by reading the literature available regarding the subject or by inspection; he should have learned it by personal experience. He should have direction not only of the planning but also supervision of the execution of the work.

The architect should also be experienced in the mechanical, electrical and sanitary equipment of a hospital, possibly not in the final details of their installation but his office organization should embrace men expert in these things, which are of such vital importance to success in the operation of a hospital both medically and economically.

In carefully studying the origin and progress of existing hospitals, it is often found that they are a composite of several parts, to the detriment of their patients. Enlargements and additions, sometimes small occasional additions, sometimes in important new buildings, without uniformity or in violation of the original basic ideas. There are a few

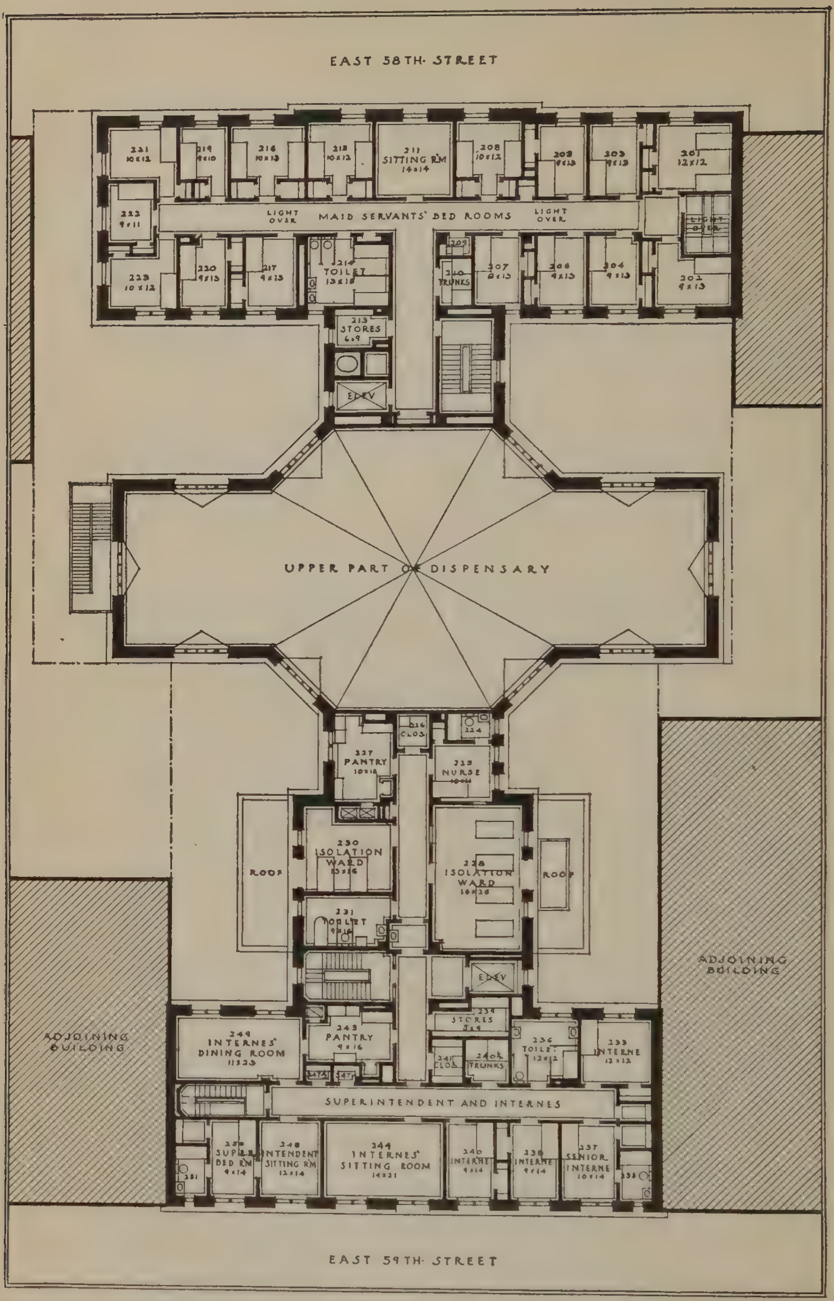


FIG. 194.—Second floor, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

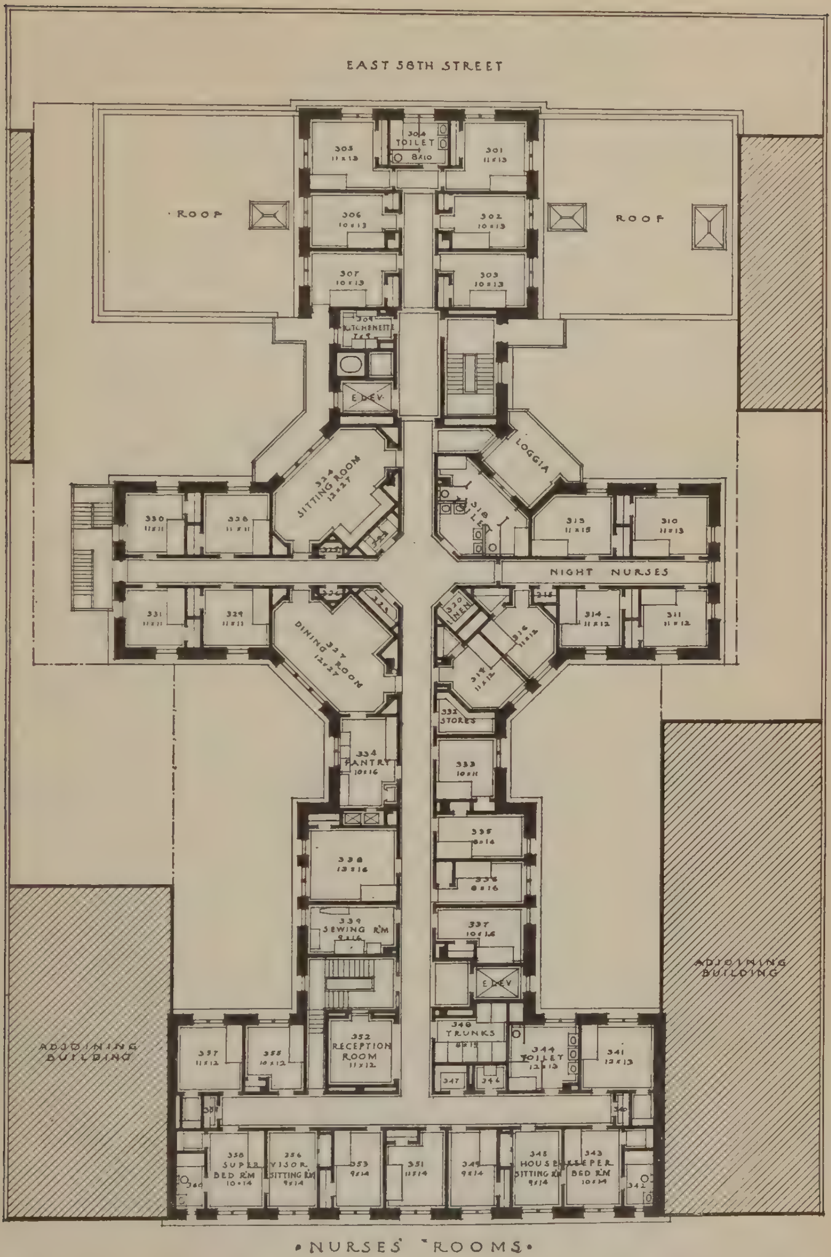


FIG. 195.—Third floor, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

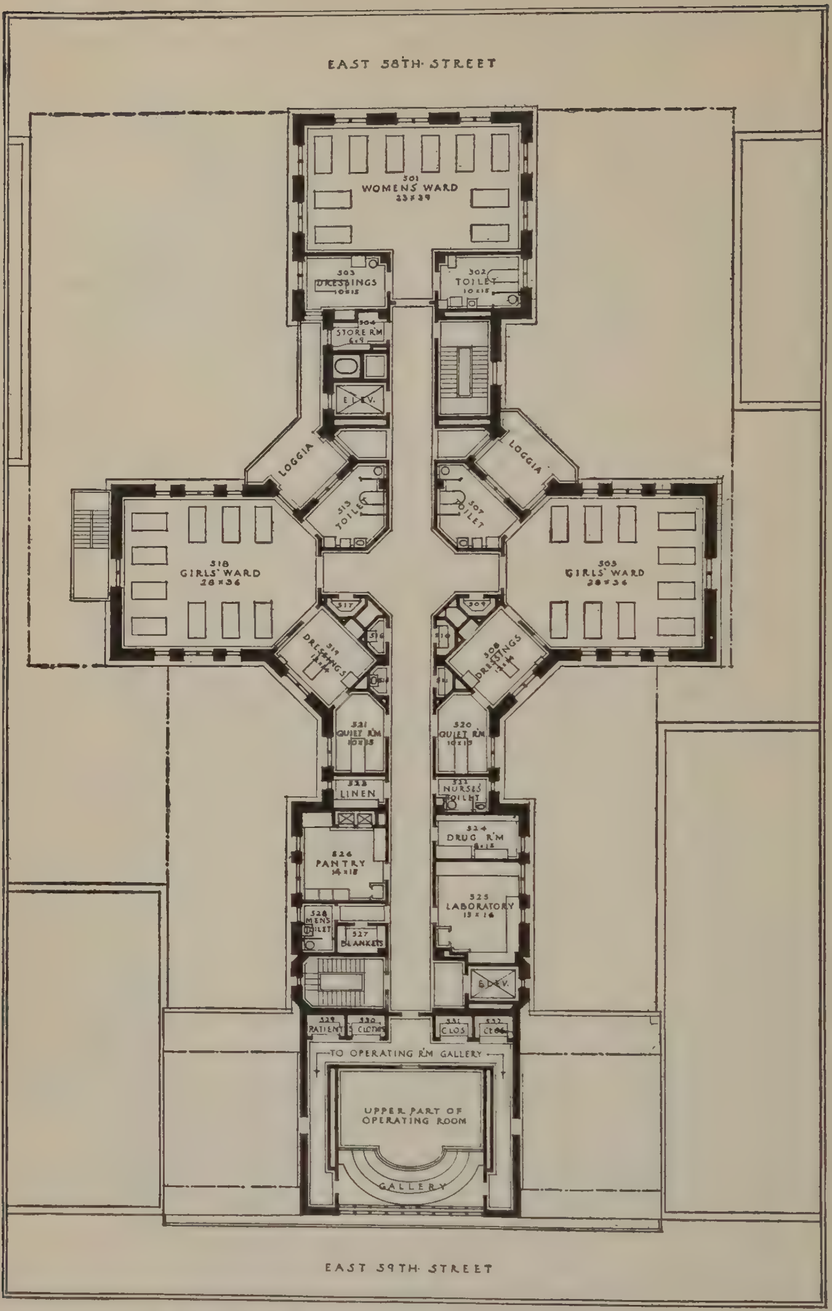


FIG. 196.—Fifth floor, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

examples in which trained minds have succeeded in recasting the whole character of the basic ideas, but usually the results are a failure. This does not refer to the architectural character of the building, but solely from the standpoint of the hospital superintendent and hygienist.

Site.—In the selection of the location for a children's hospital there are a few fundamental essentials:

It must be readily accessible to the patients, their friends and relatives, and to the physicians on the staff. The recent rapid improvement in road conditions in and about cities, the general use of the automobile, the "jitney" and the extension of street car lines, has considerably enlarged the range of selection for a hospital site. Accessibility, however, for children and the members of less well-to-do families means that it must be possible to get to them by the cheap means of transportation, street car, jitney or suburban train. The poor cannot afford automobiles.

The site should be well drained, more or less elevated, removed from stagnant pools of water which may serve as breeding spots for mosquitoes.

It is manifest that a children's hospital should be surrounded by the pleasantest conditions and those which will bring about the speediest cure. Such conditions require all those things which make for comfortable living and the least annoyance to the senses, *viz.*, an approach by way of well-kept streets, well-maintained buildings, preferably through a residential neighborhood; ample grounds, which will permit of securing privacy by having the buildings a reasonable distance from the public thoroughfares. Grass, trees, shrubs and other planting, freedom from smoke, odors and noises. If possible, a shaded grove where the patients may be out of doors with comfort during the hot weather. This will require that the hospital is not in an industrial neighborhood, or too close to railways, surface lines and other means of transportation.

The location should be governed by the prevailing winds, which should not pass over industrial districts in which smoke and gases originate.

It is hardly necessary to point out that the building should be so orientated that as much as possible of the exterior is bathed in sunshine for the maximum of time, that projections do not prevent the flow of air or cast shadows on other parts of the building.

There should be free movement of air (no system of artificial ventilation has been found as effective as the open window properly guarded), but with protection from high winds, smoke and dust. It should be as quiet as possible, and, finally, the dimensions and topography of the site should be such as to permit of future expansion of the hospital. Not infrequently ground is offered as a hospital site by some philanthropic citizen. However well meant such an offer may be, it should not be accepted by the Board unless it meets, in a reasonable degree, these conditions.

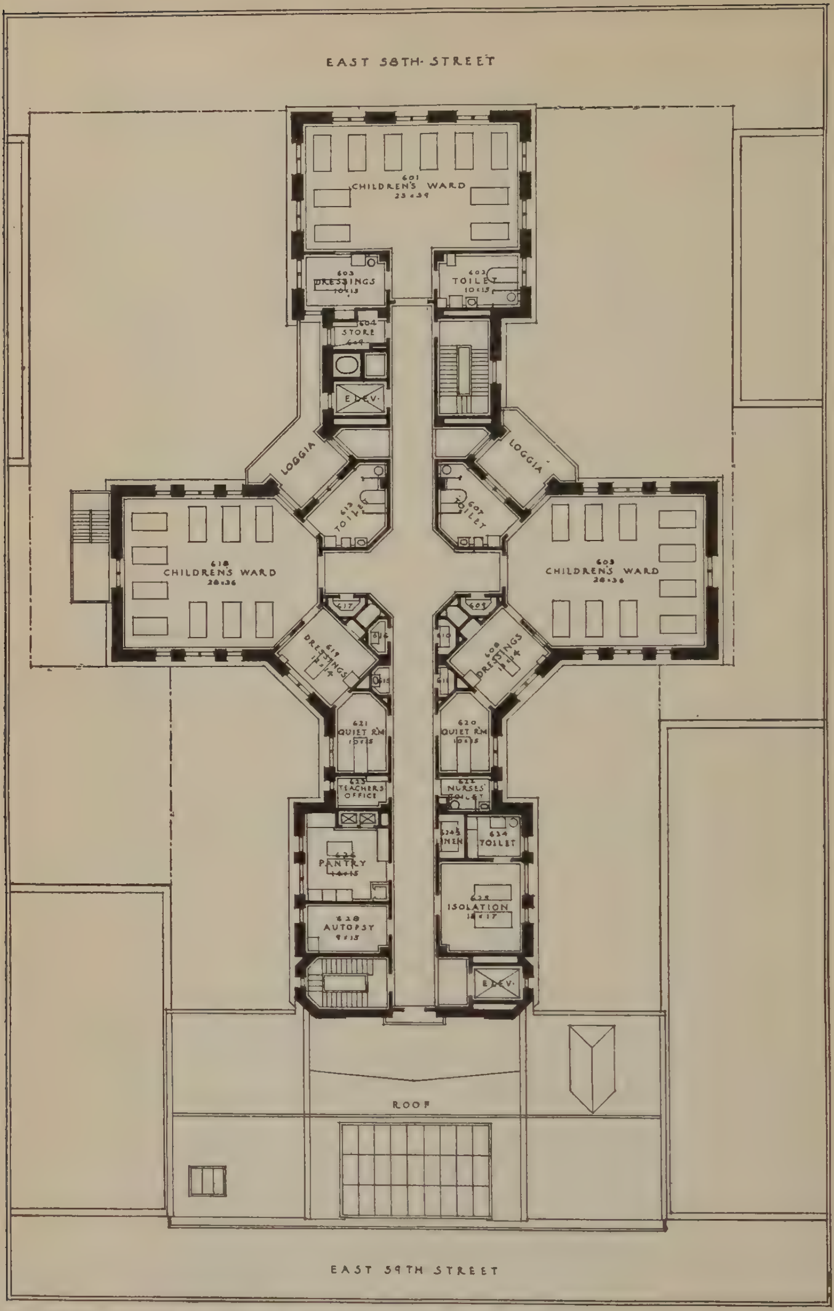


Fig. 197.—Sixth floor, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

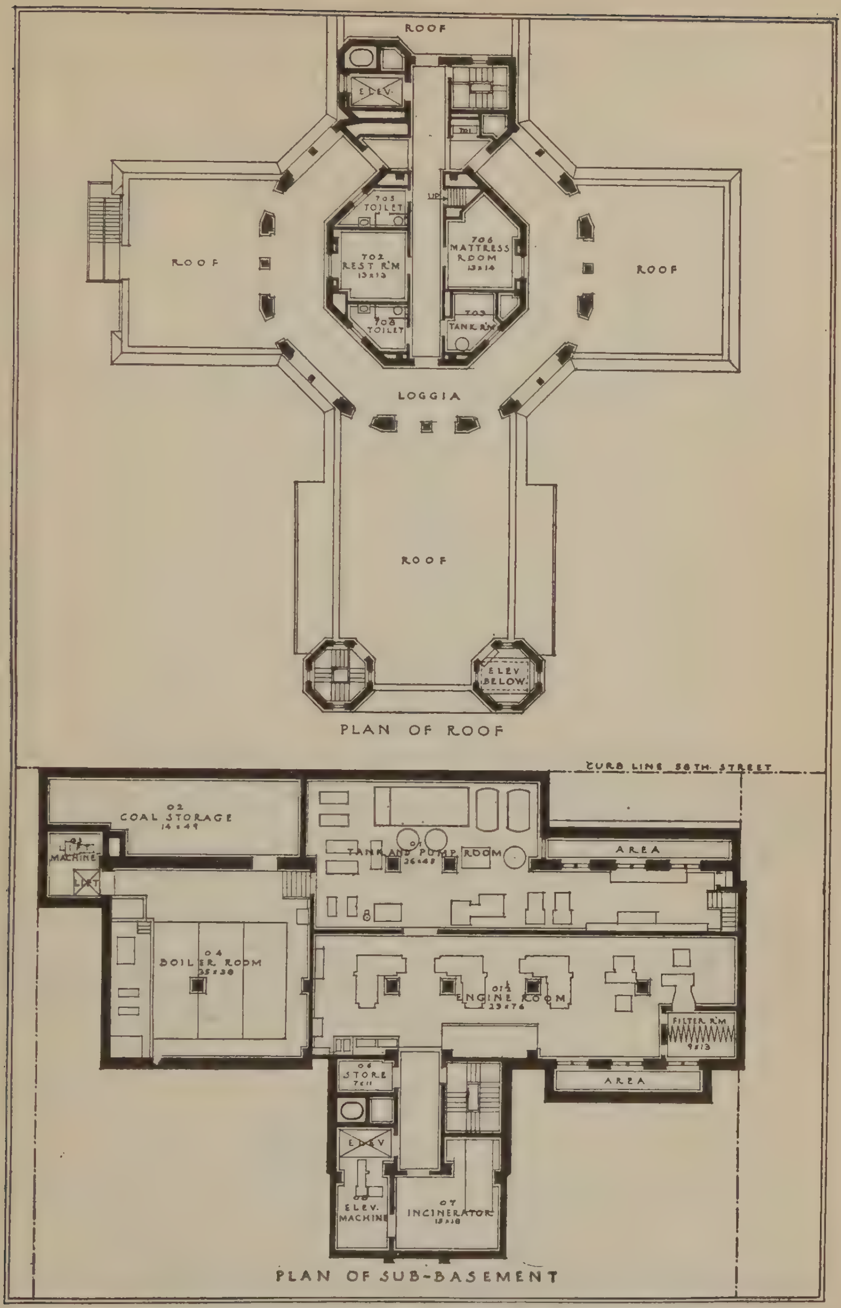


Fig. 198.—Sub-basement and roof, New York Orthopedic Dispensary and Hospital, New York City. (York and Sawyer, architects.)

The orientation should permit of many porches, or solarii, in close proximity to the various wards that patients may be placed on these with facility and close to their respective wards to avoid breaking up a unit or group or making it necessary to place the patient in charge of another nurse than the one which generally has charge of the patient at times when the patient is in a solarium.

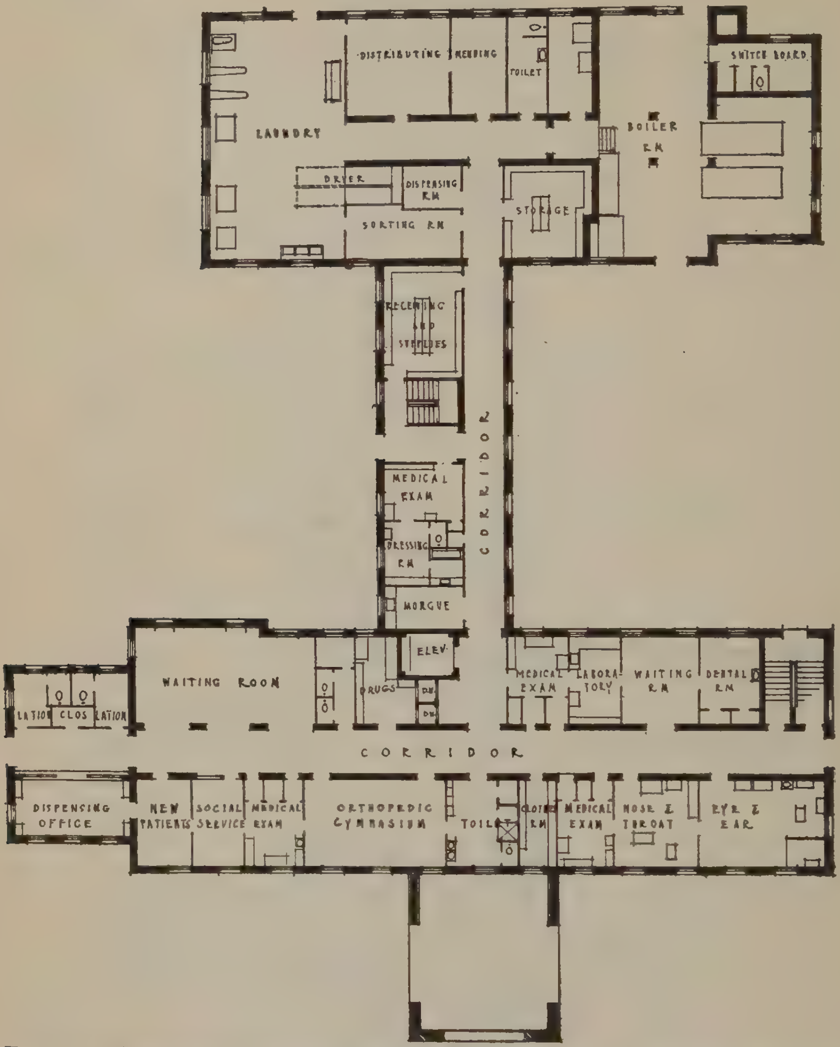


Fig. 199.—Basement, Children's Hospital, Columbus, Ohio. (Richards, McCarty and Bulford, architects.)

Low buildings are more desirable than high buildings on account of easier access to gardens. It is obvious that about one-half of the total number of patients in a two-story hospital can have direct access to surrounding grounds and that the proportion decreases rapidly when the height of the building is increased. In a small hospital say not over 100 beds, a single building will suffice, but in institutions of much larger capacity it would be better to divide the hospital into several pavilions or cottages. A complete segregation into units does not increase the cost of operation or the cost of the group and assures safety against cross infection or contagion of the whole population.

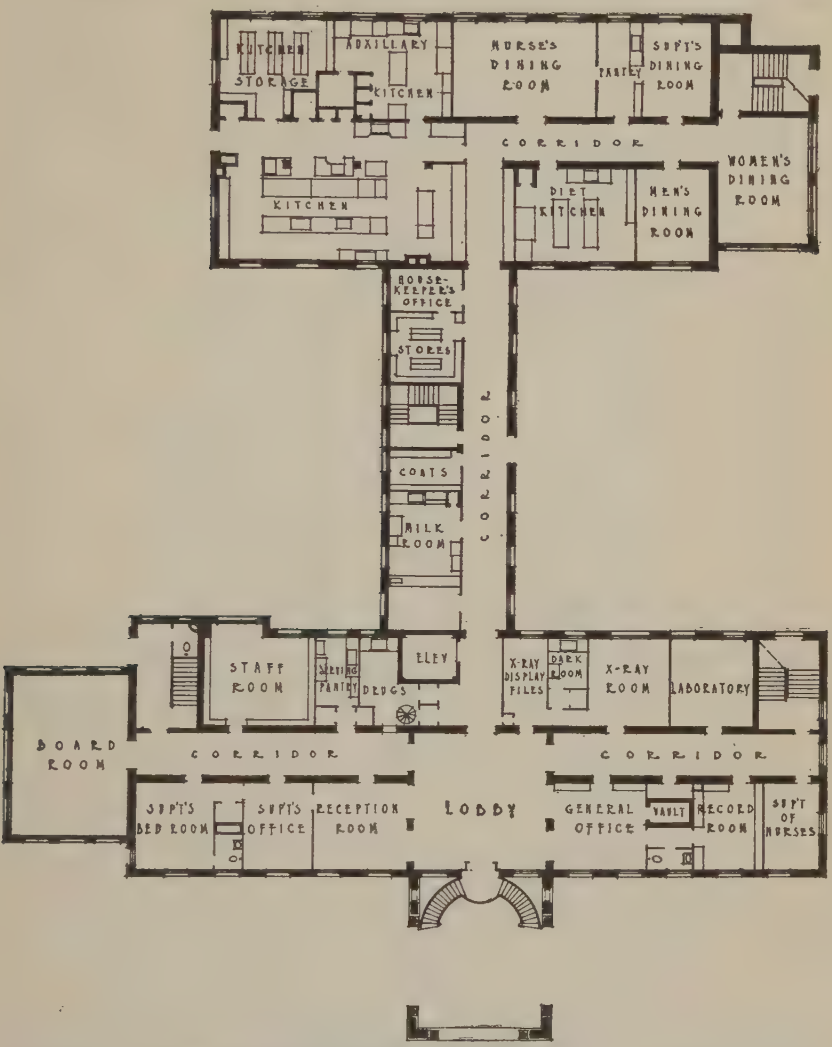


FIG. 200.—First floor, Children's Hospital, Columbus, Ohio. (Richards, McCarty and Bulford, architects.)

Notwithstanding that an ideal such as outlined above cannot be realized in every instance, inasmuch as it is especially difficult to realize it in our cities, it will not always be possible to obtain it, but land costs are the least part of the cost of the hospital and large areas should be obtained.

Children's hospitals should not be placed in a congested area and as land values in such areas are greater than in many residential or suburban districts, it would seem much better to avoid congested areas and locate the institution in one in which the ideal can be obtained.

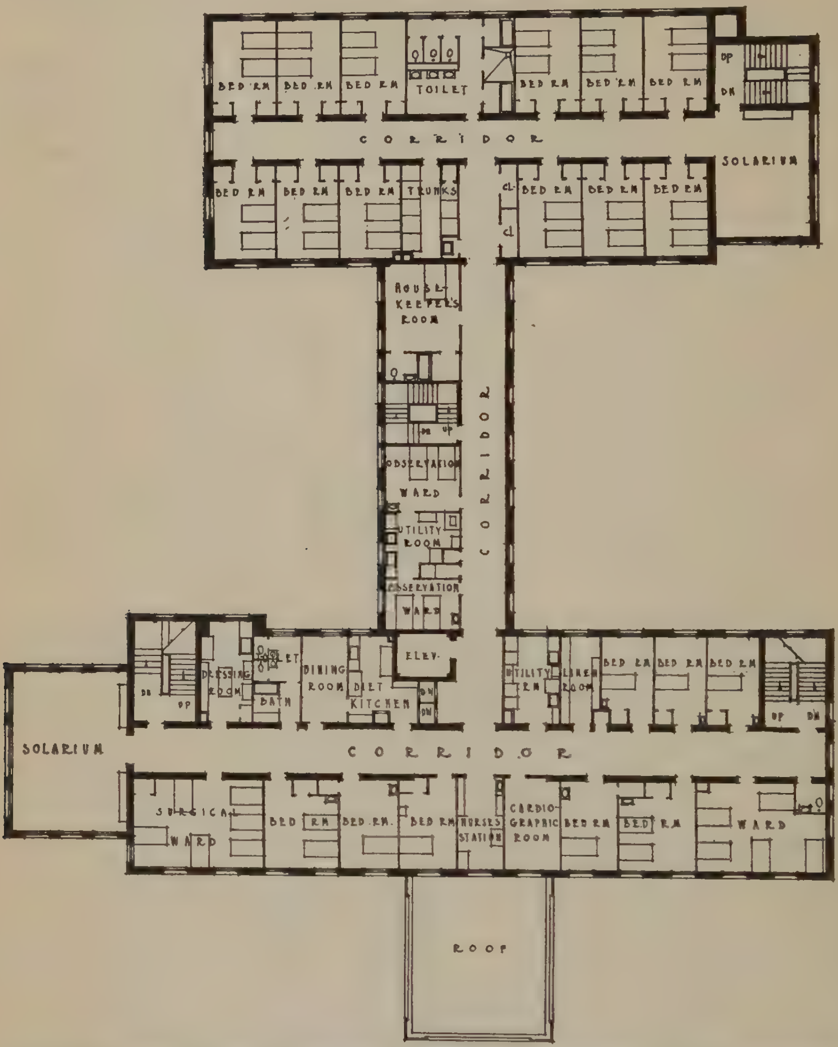


FIG. 201.—Second floor, Children's Hospital, Columbus, Ohio. (Richards, McCarty and Bulford, architects.)

In these days of rapid transit, the objection to placing a hospital at a distance from the homes of parents and physicians has but little weight.

The Children's Department of a General Hospital.—Only in the larger cities, as has already been said, are independent separate hospitals for children and infants to be advised. In the vast majority of cities, the number of sick children is not large enough to warrant the maintenance of a hospital devoted exclusively to them. In these smaller cities, the need is best met by the provision of a department for infants and children in a general hospital, preferably in a special pavilion; if not, on separate floors, as completely separated from the rooms and wards for adults as it is possible to provide. The pediatric medical staff should be composed of physicians who are giving their attention exclusively to pediatrics. What has been said in reference to the separation, in the children's hospital, of infants from older children, of medical from surgical patients, and of the two sexes, among the older children, applies likewise to the Children's Department of a

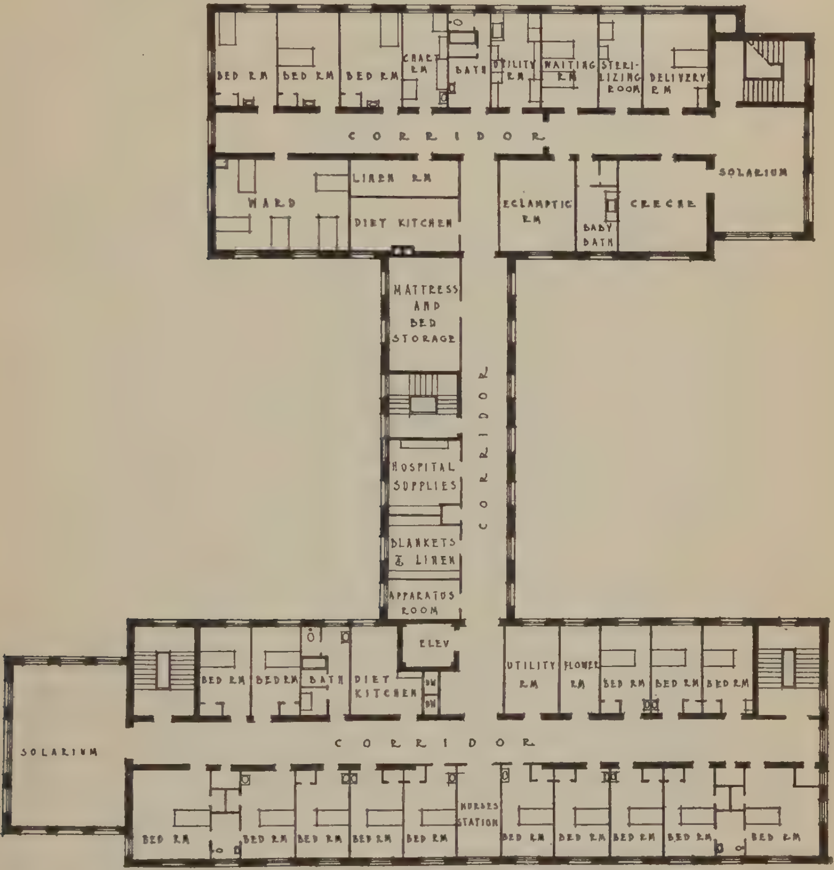


FIG. 202.—Third floor, Children's Hospital, Columbus, Ohio. (Richards, McCarty and Bulford, architects.)

general hospital. To what degree this desirable segregation of these several clases of patients can be provided for will depend largely on the size of the pediatric department.

The Hospital Buildings.—In designing a Children's Hospital, the plans must include:

I. Accommodations for patients in single rooms, wards or both, with separate provision for:

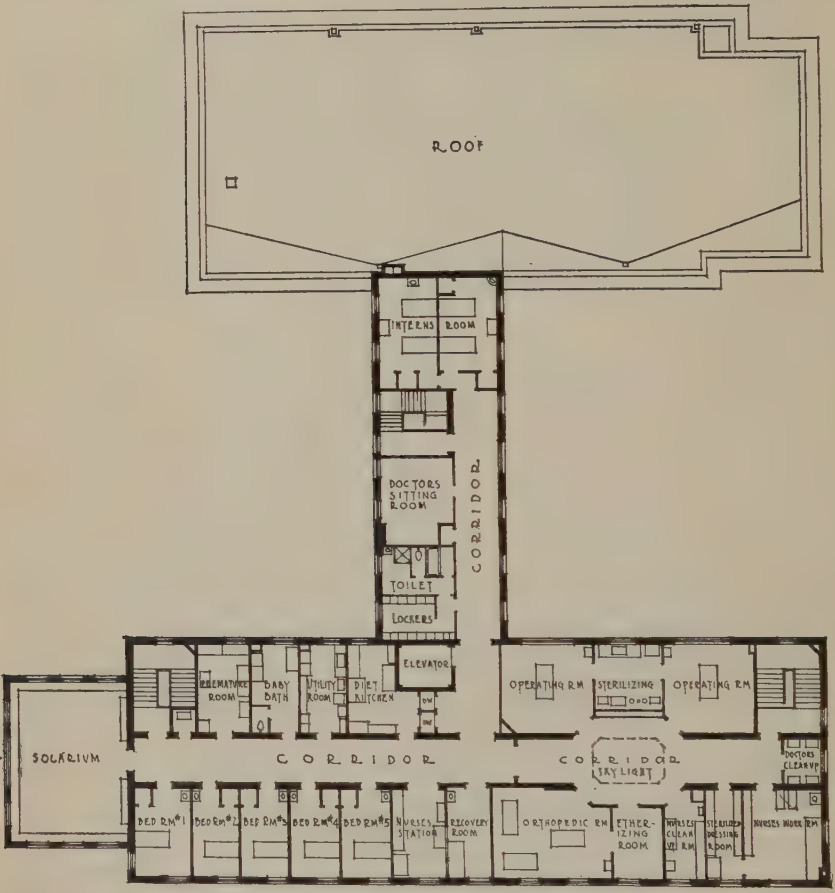


FIG. 203.—Fourth floor, Children's Hospital, Columbus, Ohio. (Richards, McCarty and Bulford, architects.)

(A) Infants.

(B) Older children as follows:

1. Observation or detention wards or rooms.
2. Wards for the longer stay of patients, and to which they are transferred from the observation wards.
3. Isolation rooms or wards for cases of communicable disease which develop in the hospital.
4. Special rooms for very sick patients.

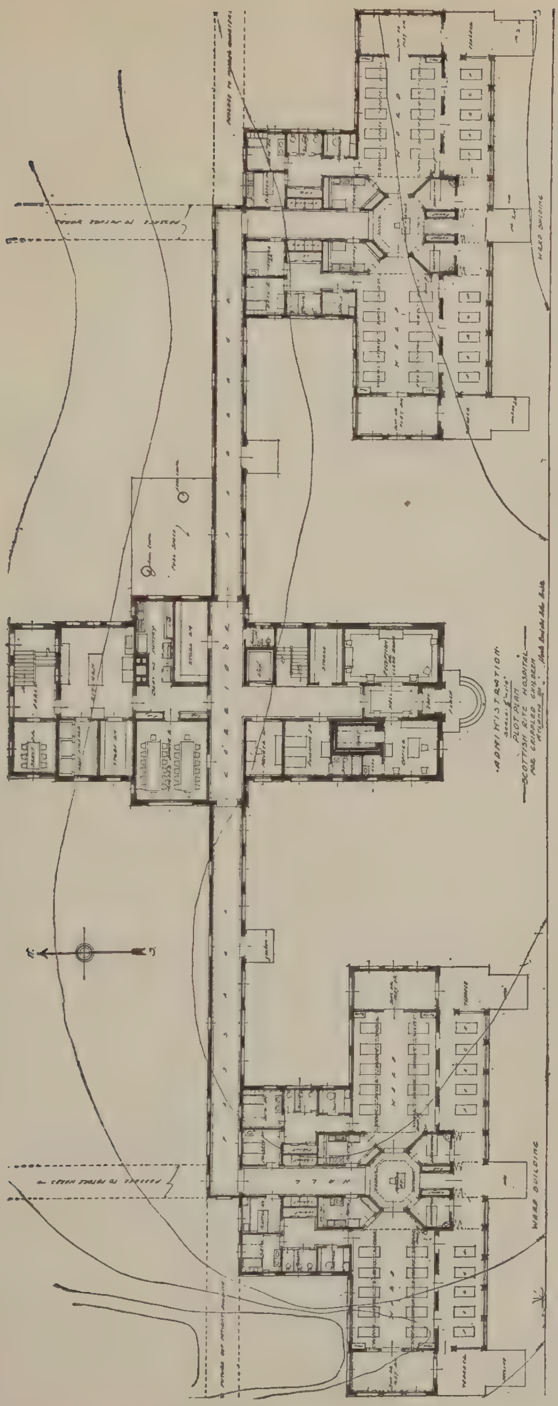


FIG. 204.—Second floor, Administration Building, Scottish Rite Hospital for Crippled Children, Atlanta, Ga. (Hentz, Reid and Adler, architects.)

In connection with these quarters for patients, there must be the necessary diet kitchens, bath rooms, toilets, duty or service rooms, and linen closets. Convenient to every ward or group of rooms there should be an open porch (not a solarium) so that all of the patients whose condition doesn't forbid may be out of doors for some portion of the day. The roof of the hospital is the best possible location for such out-of-door sojourn of the patients, but unless it is readily accessible from the wards, and certain nurses are deputed to take the children to the roof garden for stated periods, it is likely to remain unused however admirably the roof space may be arranged and equipped for this purpose.

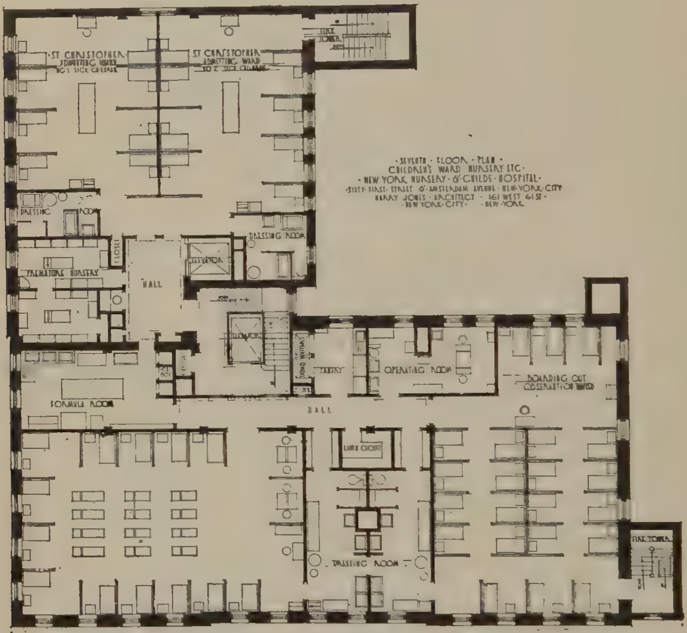

· SEVENTH · FLOOR · PLAN ·
CHILDREN'S WARD NURSERY ETC ·
· NEW YORK NURSERY · & CHILDS · HOSPITAL ·
· SIXTY · FIRST · STREET & · AMSTERDAM AVENUE · NEW YORK · CITY
HARRY JONES · ARCHITECT · 161 WEST 61 ST ·
· NEW YORK · CITY · · NEW · YORK
ST CHRISTOPHER ADMITTING WARD
ST CHRISTOPHER ADMITTING WARD
DRESSING ROOM
DRESSING ROOM
PREMATURE NURSERY
CLOSET
HALL
ELEVATOR
FORMULA ROOM
PANTRY
OPERATING ROOM
BOARDING OUT OBSERVATION WARD
HALL
LINEN CLOSET
DRESSING ROOM
FIRE TOWER
FIRE TOWER

FIG. 205.—Seventh floor, Children's Ward, Nursery, Etc., New York Nursery and Child's Hospital, New York City. (Harry Jones, architect.)

II. For the nurses, there must be ample accommodations for living in comfort, when off duty, and these are best provided, for a large hospital, in a separate building not too far removed from the hospital. In this building, as a rule, can be installed the neessary classrooms and laboratories for the instruction of the pupil nurses.

III. For the Medical Staff.—(*a*) For the physicians of the resident staff (residents and internes), comfortable living rooms, dining room and recreation parlor, in convenient proximity to the wards. (*b*) For the attending staff, a coat room with lockers or other appliances for outer clothing, with toilet room. (*c*) Pathological laboratory; (*d*) *x*-ray laboratory; (*e*) library, and adjacent thereto, filing room for

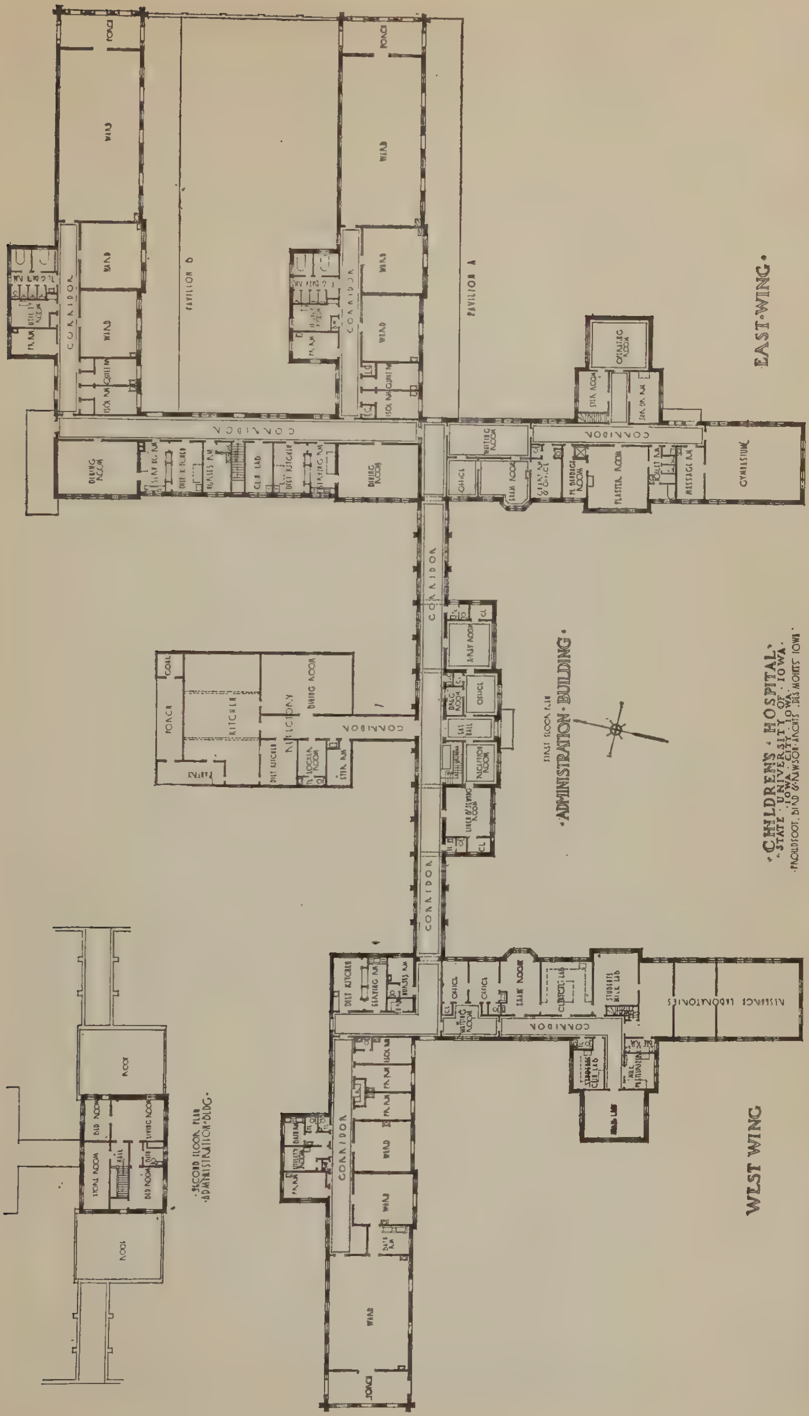


Fig. 206.—Children's Hospital, State University of Iowa, Iowa City, Iowa. (Proudfoot, Bird and Rawson, architects, Des Moines, Iowa.)

clinical records, and of advantage is (*f*) a medical staff dining room, which will encourage frequent coming together of the staff members.

IV. Administration.—(*a*) Living quarters for the Superintendent and family; (*b*) offices for the Superintendent, Room Clerk and Book-keeper.

V. Pharmacy or drug room.

VI. Living quarters for the non-professional personnel, cooks, maids, laundry workers, etc.

VII. Power plant.

VIII. Laundry

IX. For the patrons of the hospital, (1) reception room, with examining room (bath room and toilet adjacent).

X. Rooms for the Out-patient Department, including waiting rooms, examining rooms for the several departments, pharmacy, laboratory, offices for the social service workers, and clinical record room.

To discuss some of these items more in detail:

I. Infants should be entirely separated from older children, because they require a very different kind of care and nursing, different diet, higher room temperature, and, moreover, because they are very susceptible to communicable diseases so frequently brought into the wards by older children. Infants, rather better than older children, can be well cared for in wards of from 6 to 12 beds. Much larger wards than this are to be found in many hospitals for children, but experience has shown that the smaller wards have decided advantages and the trend of opinion in recent years has been undoubtedly toward the smaller wards and single rooms.

In connection with the infant department there should be provided a special room for prematurely born infants, where the number of patients of this type is sufficiently large to warrant such a room. The very best of incubators, so largely used for such patients, are unsafe, both as to temperature and ventilation, unless they are closely and constantly watched by a careful, conscientious nurse. With such care, very good results can be secured in any hospital room or ward, or even in a private home, without the incubator. Much the most satisfactory plan is a special room which can be kept constantly at the higher temperature required, while at the same time perfect ventilation insures an ample supply of oxygen. Oxygen is as indispensable for the nutrition and metabolism of the infant as is food.

II. (1) The purpose of an observation (also called a detention or receiving ward) is to minimize, in so far as possible, the introduction and spread of communicable disease, a not infrequent occurrence and the dreaded *bete noir* of every children's hospital. The development in a ward of a case of measles, diphtheria, pertussis, gonorrheal vaginitis or other infectious disease exposes every other child in that ward to an attack of the disease and compels the quarantine of the ward for a period of at least three weeks and often twice that period. Even when cases of different highly infectious diseases are in adjacent beds in the same ward; but this is possible only with a permanent corps of experienced nurses, and with attending medical men of long training. Such a nursing corps can be had only at an expense which is prohibitive for most hospitals. Where the nursing is done by pupil nurses, who are assigned to duty in the children's wards for short periods only, usually two to four months, it is impossible to secure that high degree of caution which will prevent the spread of contagion. If a case of communicable disease developes in a ward under these conditions, there is great probability of its transmission to other children in the ward.

In most hospitals, therefore, it has been found of advantage to assign the new patients to an observation ward, for a period of from two to three weeks. Such wards should be small, containing not more than six beds, best of all are single rooms. Partial separation of the beds by glass partitions projecting from the wall to just beyond the end of the beds, and from 6 to 8 in. above the floor to a height of 5 or 6 ft., (the cubicle plan) serve as a reminder to the nurse that each patient is to be handled as a potentially contagious case and offer considerable protection against the spread of contagion by mouth spray in coughing and sneezing.

FIG. 207.—Orthopedic Hospital, Research and Educational Hospitals of the State and University of Illinois. (Richard E. Schmidt, Garden and Martin, architects.)

Visiting of Patients by Relatives and Others.—It would conduce much to the welfare of children who are sick in the hospital,

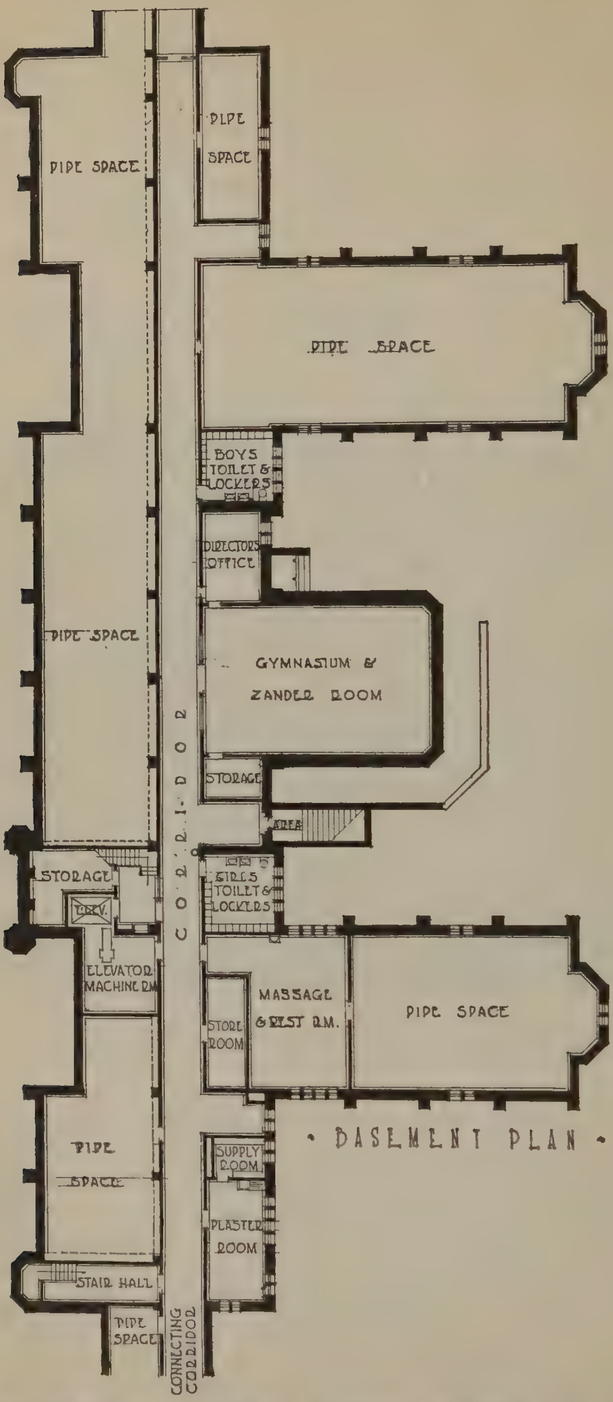


FIG. 208.—Basement, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

if visiting of these patients by the mother and other members of the family could be entirely abolished. Some hospitals have such a rule, but the enforcement of such a regulation is resisted by many mothers and they will not allow their children to be taken to a hospital unless they are allowed to visit them. In a good many instances these mothers can be made to see that such visits by the mother or any member of the family are detrimental to the patient. Most children, although they may be at first disturbed by the transfer from home to hospital, soon become reconciled and contented. Each visit from a member of the household, however, recalls the home, the departure of the visitor is likely to be followed by a crying spell on the part of the patient, with sometimes an aggravation of its symptoms. Every effort should be made by the attendant physician and the nurses to dissuade the mother from visiting her sick child in the hospital, but it is not always wise to rigidily enforce a rule against all such visiting. Often the mother can be persuaded to forego such visits if arrangement is made by which daily or less frequent reports are made to the family by telephone as to the condition of the patient. In arranging for such reports it is well to have a definite hour set when the family are to telephone the interne or nurse. If all such telephone inquiries are set for a definite hour of the day, two to five minutes being assigned to each, it will promote prompt service on the telephone and reduce to a minimum the time required of the interne or nurse.

When such visiting is permitted, the patient should be taken to a room provided for that purpose, the mother or other visitor (only one should be allowed at any one time) should be required to put on a clean hospital gown, to see the patient only in the presence of a nurse and for only a few minutes (15 at the most) and not to handle or come in close contact with the child. Only by such precautions, thoroughly carried out, can the occasional introduction of contagious disease be avoided.

It is hardly necessary to say that parents should always be notified promptly in case of a change for the worse in the condition of their child, and especially if a fatal issue seems imminent.

Isolation Rooms.—A patient who develops a communicable disease should be promptly removed from the ward to an isolation room or ward, or, better still, to a hospital designed for such cases, if there be one available.

Internes and Nurses Quarters.—Comfortable and quiet sleeping rooms for nurses and internes are essential, in justice to them and the interests of efficient service. Equally important are provisions for recreation, both within and out-of-doors. A tennis or hand-ball court in the hospital grounds is a standing invitation to wholesome and needed out-of door exercise.

Dining Rooms.—A dining room for the medical staff, including the residents and internes, is a particularly effective means of bringing about frequent contact between the members of the medical group,

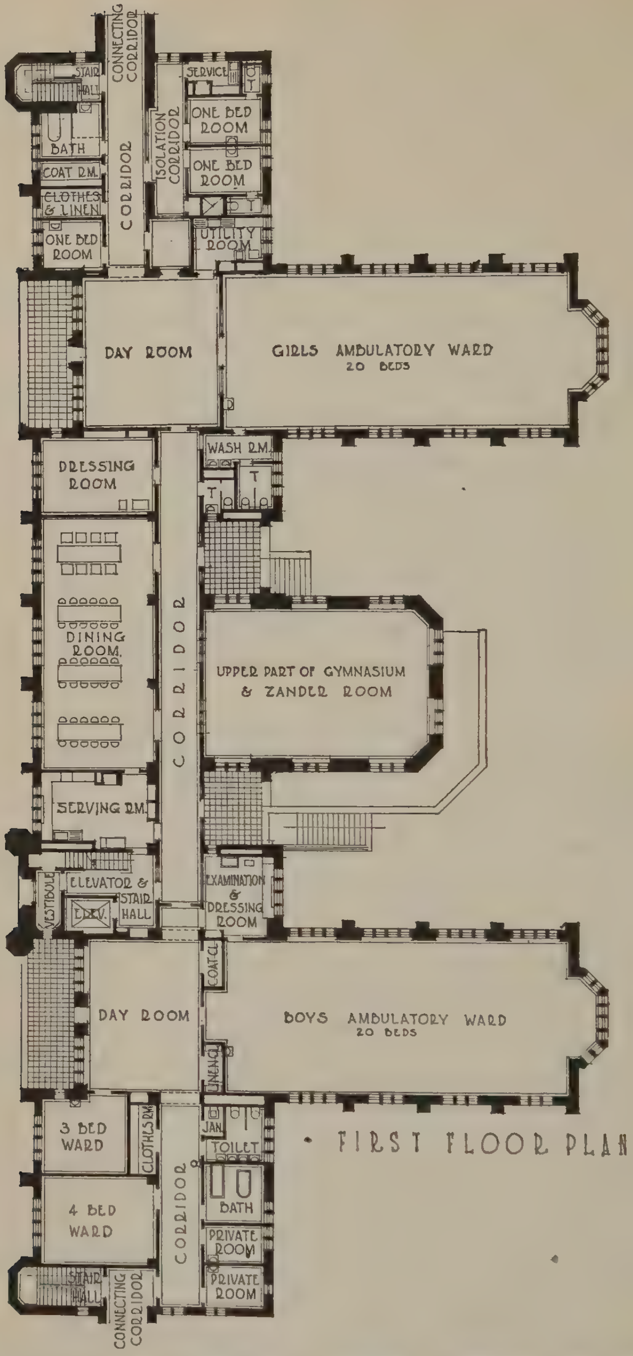


FIG. 209.—First floor, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

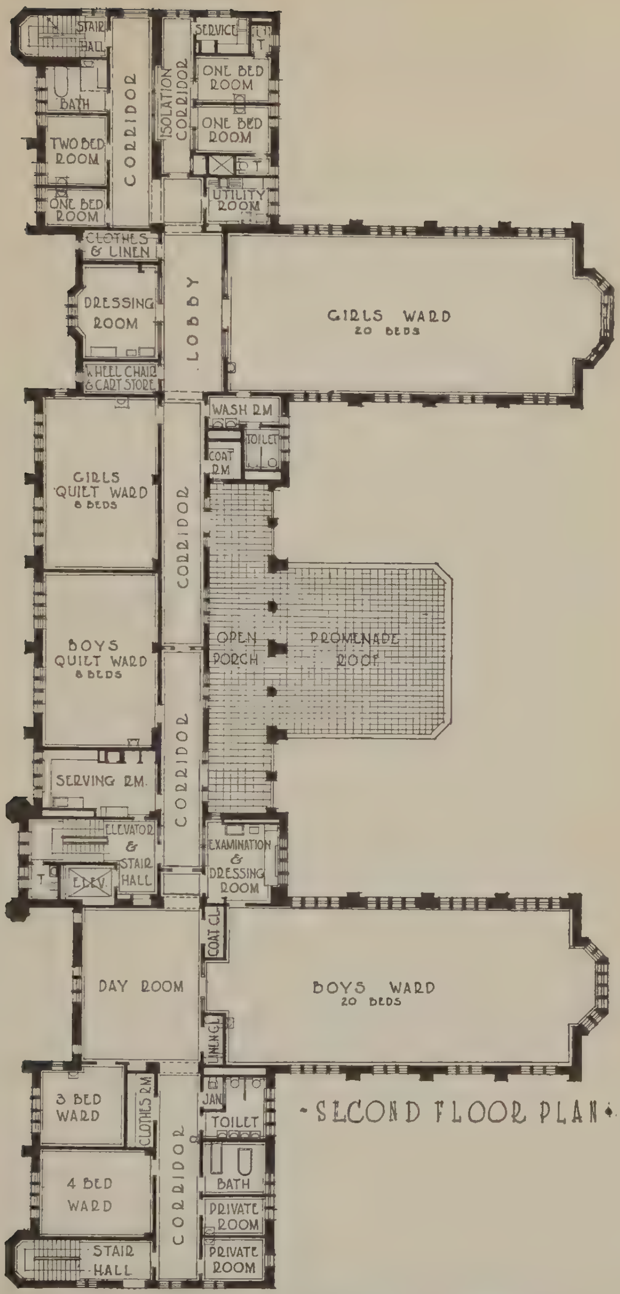


Fig. 210.—Second floor, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

and securing for the internes the most helpful sort of social and professional intimacy with the members of the attending staff. A considerable number of this staff should be induced to take the midday meal at the hospital each day.

Laboratories.—It is scarcely necessary to emphasize the importance of adequate, well-arranged and well-lighted rooms for the laboratories, so placed as to be as accessible as possible to every ward or room.

In a large hospital a small laboratory on each floor, in addition to the main laboratory, is a great convenience. In these smaller rooms much of the routine laboratory work can be done by the internes.

Diet Kitchens.—The diet kitchens are usually provided for each floor of the hospital, in addition to the main kitchen where food is prepared for the patients who are able to go to the patients' dining room, as well as for the working force of the hospital. There are distinct advantages, however, in a large hospital in locating all diet kitchens in the general kitchen, so that all the food prepared in the house may be under the direct supervision of the dietitian, an indispensible functionary of the modern hospital. The food, here prepared, is sent to the wards and rooms in heated containers by carriers and dumb waiters. Such a centralization of the matter of food preparation and distribution simplifies and makes more effective the work of the dietitian and her assistants, promotes economy in the purchase and preservation of supplies and tends to avoid wastefulness. Moreover, the dietitian can give practical instruction to the nurses to better advantage in such a centralized kitchen than in small kitchen units located at several different places in the hospital.

The dietitian, or, in a large institution, one of her assistants, should inspect every tray or nursing bottle that is sent to the patients, and inspect them also when they are returned from the wards or rooms. One of her most essential duties is to know when food is returned, wholly or in part, uneaten, and to inquire at once into the reason therefore. Frequently such an occurrence demands a conference between the dietitian, the nurse and the attending physician.

Linen Rooms.—Similarly it has been found of advantage tohave all of the linen supplies of the hospital, sheets, pillow slips, towels, napkins, diapers, gowns, etc., kept in one central place, under the charge of a competent woman who inspects every article as it is returned from use for slight rips or tears, and sees that these are promptly repaired before the articles are again used. The saving in the linen expenses of a large hospital under such a plan is a very considerable item in the annual budget.

Reception Rooms.—The reception room for patients in the hospital, and the waiting room in the Dispensary or Out-patient Department, should be so arranged as to avoid close contact of new patients. Not infrequently children are brought to the hospital by ignorant or careless parents or relatives, suffering from some communicable disease. It is unpardonable to expose other children to the

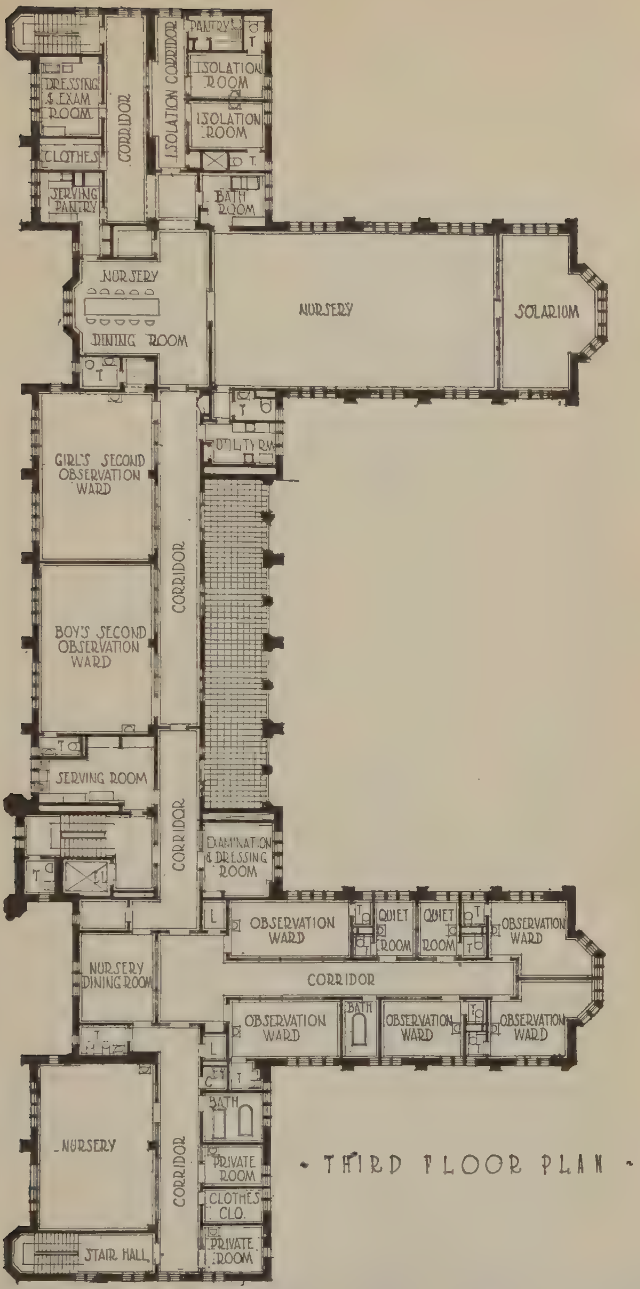


FIG. 211.—Third floor, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

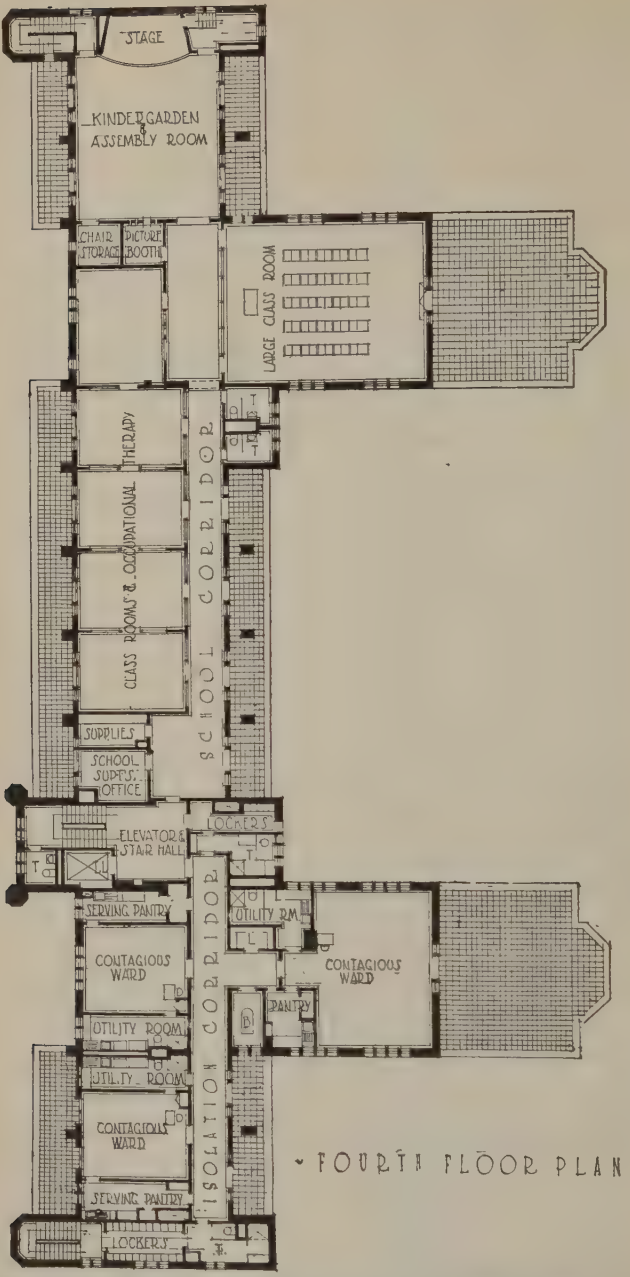


FIG. 212.—Fourth floor, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

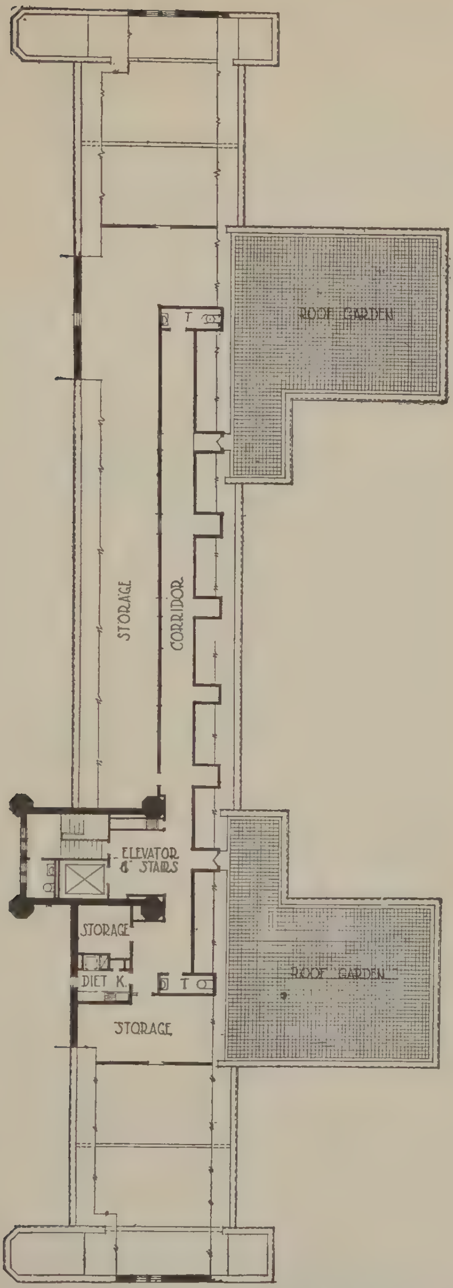


FIG. 213.—Fifth floor, Orthopedic Institute, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

possibility of acquiring contagion from such patients by close contact with these afflicted children. An arrangement of stalls, separated by partitions of wood or glass, in which each patient, or the mother with her own children are required to wait until called to the examining room, will usually avoid the exposure of other children. In the dispensary waiting room, especially, there should be a competent nurse or other attendant in charge of the room, to see that the children are kept separate. Of course every effort should be made to detect the presence of communicable disease in every new patient at the admission desk, but, even when this is in charge of a physician it is not always possible to detect every case. It is not an infrequent occurrence, even in a well-regulated dispensary, for the attending physician to find diphtheria, scarlatina, measles, varicella, pertussis or mumps.

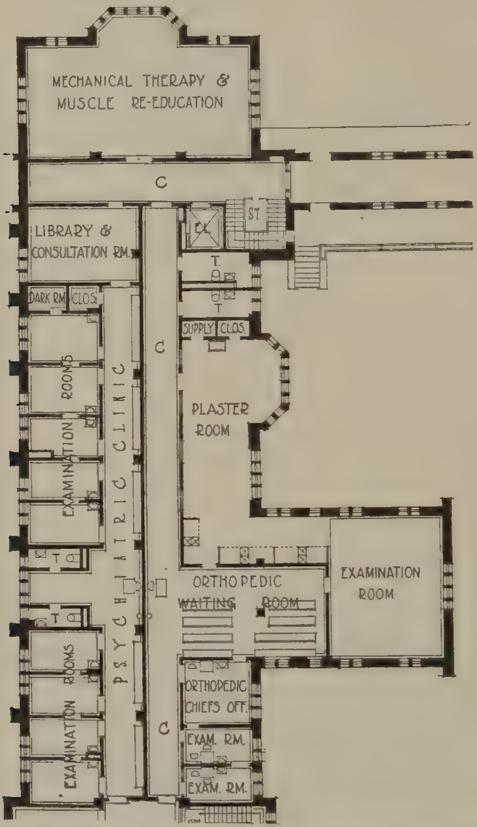


FIG. 214.—First floor plan, Out-patient Department (on the right) Orthopedic section, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

Social Service Rooms.—The rooms for the Social Service Workers are best located in the Out-patient Department. It is here that the work of social service begins, and the great proportion of the patients needing this service are from the out-patient group.

If the admission clerk is not a service worker, then the desk of such a worker should be in close proximity to the admission desk—preferably in an adjoining room, and the new patient is sent first to this point. Here the social history is elicited and recorded on the history sheet.

The rooms for the service workers should provide sufficient space and be so placed as to be convenient to the consultation rooms, in order that these workers may be in attendance on the clinics and confer frequently with the physicians. Thorough coöperation between the members of the medical staff and the social service workers is essential to secure the best results.

Convalescent Home.—In connection with every Children's Hospital of any size, it is most important to have a Convalescent Home, or Sanitarium, to which children who have reached the convalescent stage, and who no longer need the medical and nursing care which the hospital is designed to furnish, may be sent for a few days or weeks, until they have been fully restored to normal health and vigor. There are two reasons for this: First, the removal of such patients from the hospital, makes the beds available for other sick children needing hospital care, and second, the patients who have reached the stage of convalescence do much better, as a rule, if removed from the wards or rooms of even the best-managed hospital. It is a common observation, for example: That infants with gastro-intestinal disturbance—"feeding-cases"—which have been brought to the hospital for treatment, for which the proper food has been found and who have gained in weight and in other respects in an entirely satisfactory way, will, all at once, cease to gain weight and remain at a stand-still for days at a time, no

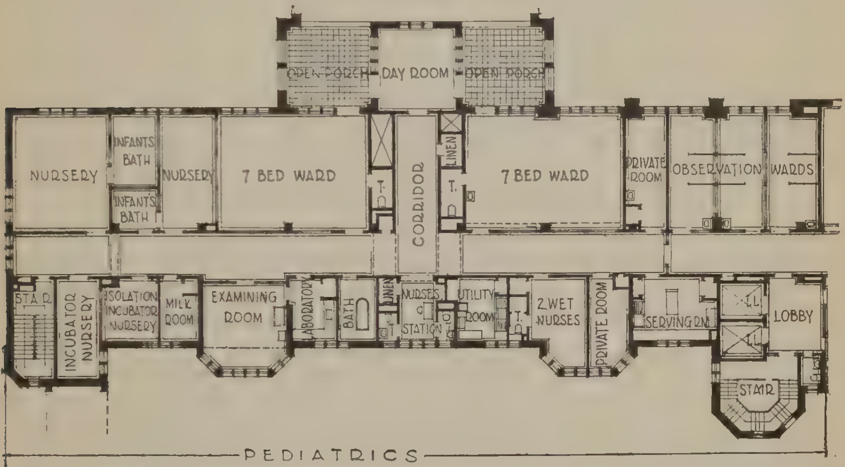


FIG. 215.—Pediatrics Department, Research and Educational Hospitals of the State and University of Illinois, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

matter what is done for them. Such patients, transferred to their own homes, if these are of the right sort, or to country Home for Convalescents, will promptly resume their gain in weight and continue to thrive. Children of the well-to-do, whose home conditions are satisfactory, do not, as a rule, need the sojourn in the Convalescent Home.

This adjunct to the Children's Hospital should be situated in the country, in the most attractive surroundings which it is possible to procure, convenient to transportation lines so as not to preclude the visiting of the patients by members of the family. There should be a visiting staff of physicians, such number of nurses as may be necessary, and, if possible, a resident physician. The duties of the resident may be discharged by members of the resident staff of the main hospital,

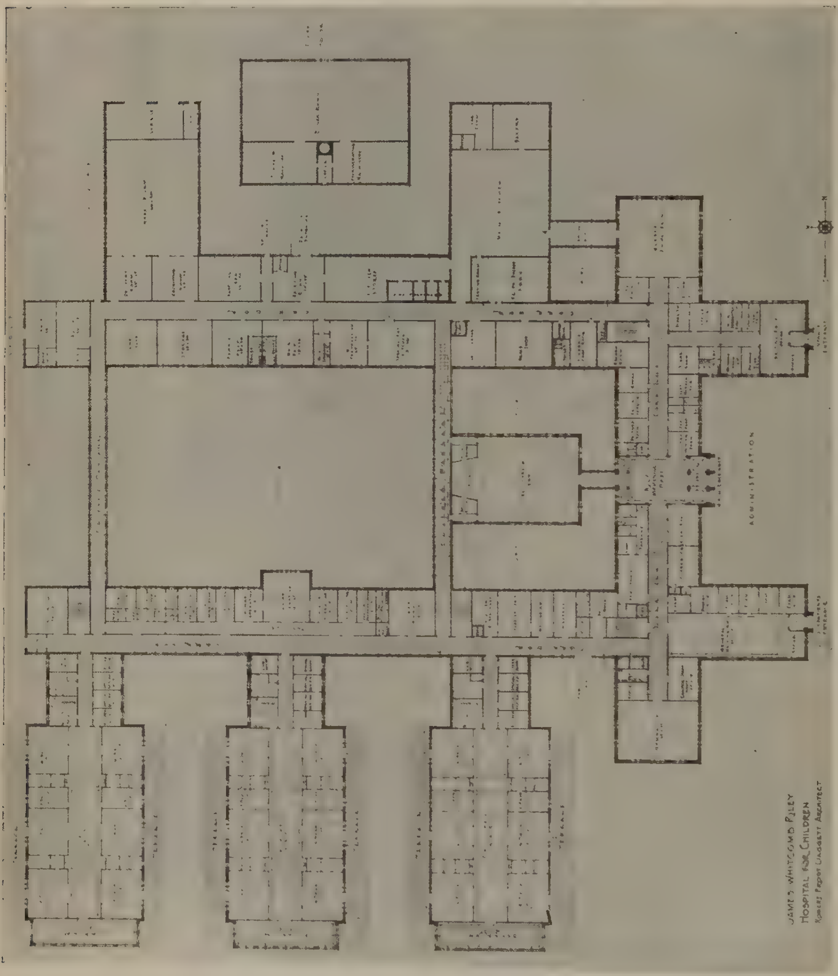


FIG. 216.—First floor, preliminary study, for James Whitcomb Riley Hospital for Children, Indianapolis, Ind. (Robert Frost Daggett, architect.)

assigned to the Convalescent Home for short intervals of three or four months each.

An alternative plan for the later care of infants is the first instituted by Doctor Chapin of New York City, which has operated very successfully. This consists in assigning one or two of these infants to a family living on a farm or in a village, not far from the city, as boarders, the mother of the family undertaking to care for these patients, for a stated compensation paid by the hospital or by some charitable organization. A visiting physician is in charge of a district and visits the patients as frequently as may be necessary. A nurse, under his direction, visits the patients more frequently, instructs the women in the care of the infants which they have taken into their homes, and reports to the visiting physician at frequent intervals.

A play room is not necessary nor advisable in a hospital for children who are actually ill. A child who has reached that stage of convalescence where he can safely be out of bed and able to play with other children, should be transferred to the Convalescent Home, or to his own home.

Hospital Equipment.—The necessary equipment of a hospital includes the fixed or construction equipment and the movable equipment.

The former term is applied to those items which are a fixed part of the building and must be provided for in its planning and construction. Among them are the appliances for lighting, heating, ventilation, laundry service and vacuum cleaning, and those for cooking and sterilizing, elevator and dumb-waiter service. These will be discussed in detail in connection with plans and construction.

The movable equipment consists of those articles which are not an integral part of the building, nor attached to it in any way, and which can therefore be moved about or changed at any time. They comprise the beds, bedding, hospital clothing, essentials for bathing the patients, utensils for the preparation and serving of food, for the writing and filing of clinical and other records, laboratory equipment and supplies, x-ray equipment, the necessary instruments for examination and diagrams, as well as those for surgical operation and for special therapeutic procedures, e.g., mechano-therapy, electrotherapy, *et al.*

These various items are described in the previous chapters of this treatise in connection with the several phases of pediatrics with which they are associated. For example: The various types of cribs and beds, are discussed in the chapter on wards; the necessary appliances for the preparation and serving of foods to the infants, in the chapters on "Artificial Feeding."

The arrangements recommended for the plan of the Children's Hospitals are presented in some of the illustrations of many of the newest buildings of this kind. Some of the plans have many of the most accepted elements, others may have only a few, however, a study of all of them is advisable.

An attempt to illustrate plans for every condition surrounding all kinds of real estate would be prohibitive and seems unnecessary, for the plans which are illustrated will be sufficient to indicate all that which should be provided.

In planning a Children's Hospital, obviously conditions must be met which do not prevail in planning a hospital for adults. The danger of contagion and cross-infection which is ever present demands special provisions to guard against them. Appropriate provisions must be made in the reception rooms and wherever the Children are placed. The arrangement of the auxiliary rooms, such as reception rooms for visitors, business offices, kitchens, service rooms, operating department and all other rooms which are not frequented by the children, will in general be similar to those required for general hospitals.

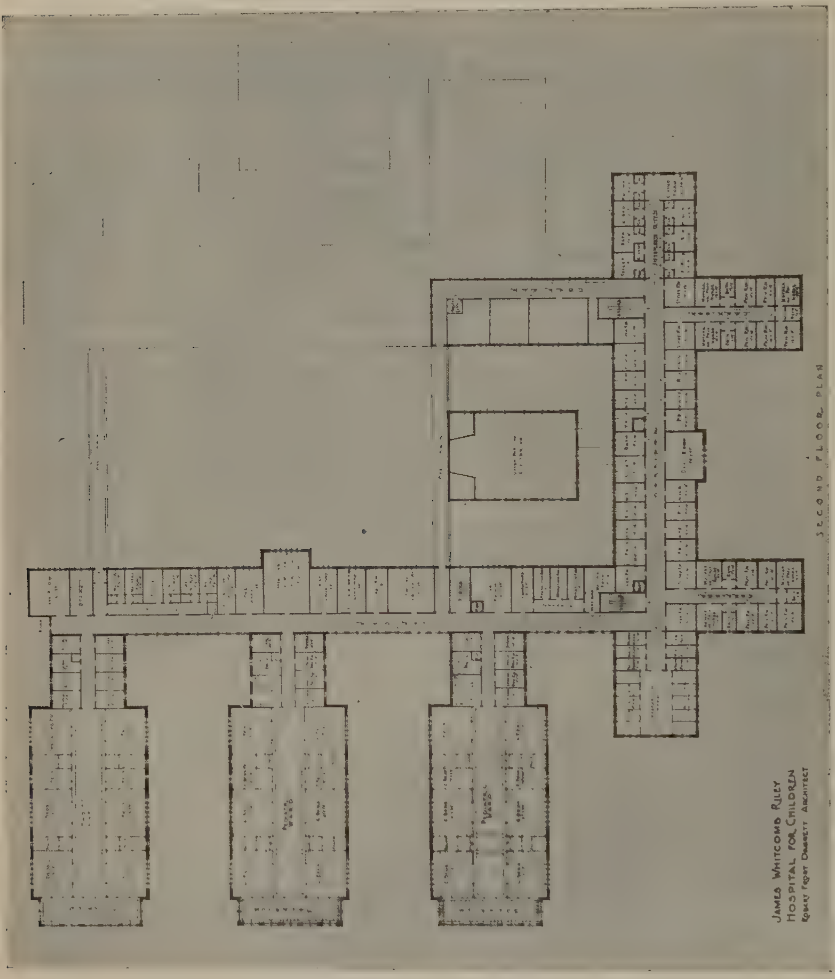


FIG. 217.—Second floor, preliminary study, for James Whitcomb Riley Hospital for Children, Indianapolis, Ind. (Robert Frost Daggett, architect.)

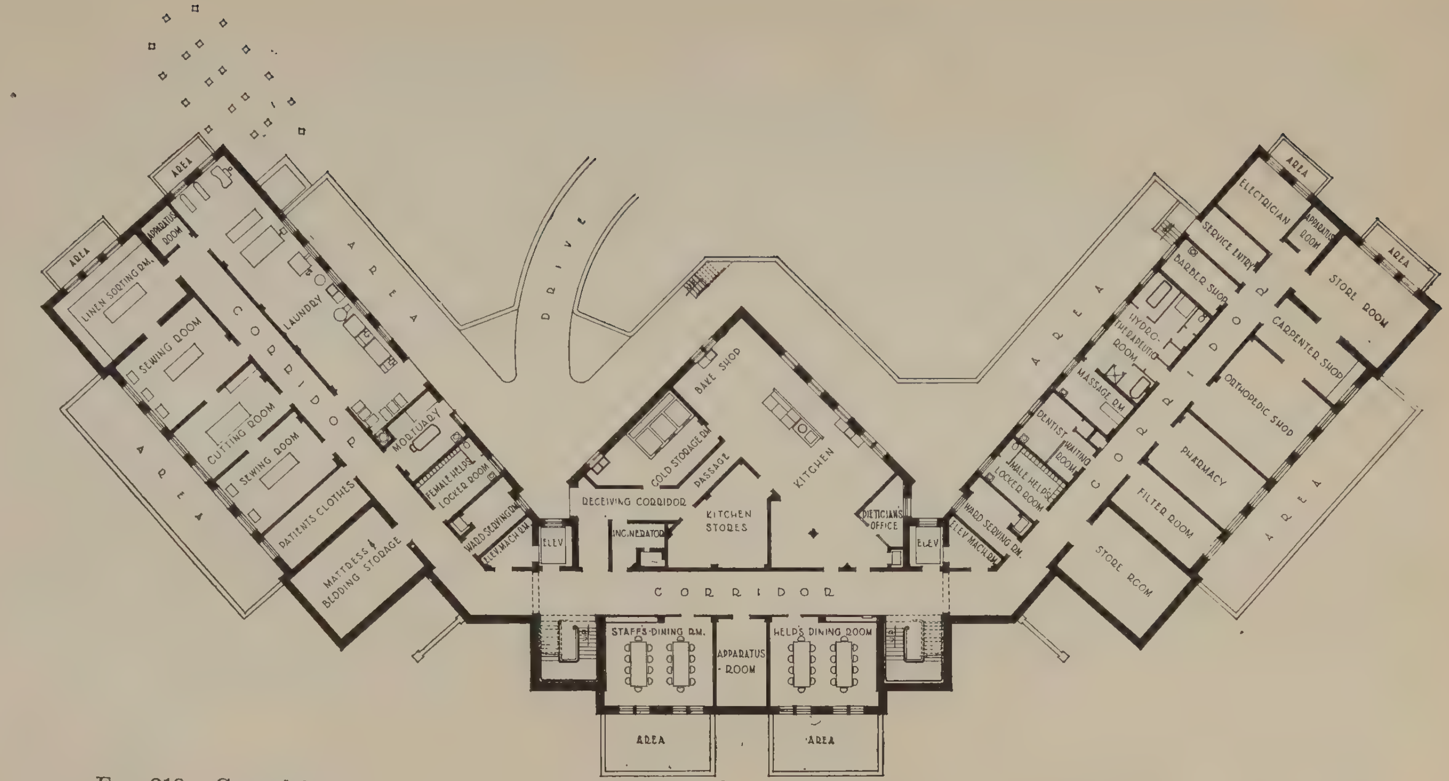


FIG. 218.—Ground floor plan, Projected Shriner's Hospital for Crippled Children, St. Louis, Mo. (Wm. B. Ittner, architect.)

Every case must be isolated until the period of incubation of the many diseases to which children are subject is passed and it is a great question if it is best to build a building having a complete department for isolation until the period of incubation has passed and other departments or wards in which the patients can be placed after that period, or, if it is better to build a hospital in which every part is so isolated that the patients can occupy the same bed during their entire stay in the hospital.

It is apparent that the first mentioned arrangement requires considerable duplication, if not almost a hospital of double the capacity of the latter arrangements.

Inasmuch as the period of incubation is almost two weeks, and the average hospital period per patient is not much more than three or four weeks, it would seem that it would be difficult to operate the first described arrangement economically.

Cubicles.—The separation in an admitting department or observation ward should be by glazed partitions dividing the space into small areas. Such areas are usually termed "cubicles" and the glazing serves the purpose of permitting observation of a number of patients by the same nurse without contact with the various patients or their beds and other furnishings. In some cases the beds are separated only by glass or canvas screens; about 7 ft. high and beginning about 10 in. above the floor. Both arrangements require the same rigid technique to prevent cross infection, cubicles by affording physical obstructioins to the attendants indicate a requirement which is not so easily omtted. In either case ample facilities should be provided for the doctor and nurses to thoroughly cleanse their hands after attending each patient. Some of the illustrations show that subdivision in the wards and an unusual number of plumbing fixtures, such as lavatories.

The most efficient partition have an upper portion of glass and the lower portion of steel. In every box or cubicle there should be two small dressers, one for the physician, one for the nurse articles used by the nurse. All dishes for the occupant, thermometer and everything necessary for the patient are kept in each box. There should be a glass shelf for toys, etc. an examination table should be placed in the middle of the ward. In some instances, everything belonging to a certain cubicle bears its number.

A metal linen closet which can be loaded from the corridor side, and a metal and glass cabinet for medicines in the upper part, lower part for bandages, etc., with heavy glass door of the cabinet hinged to form a table are convenient pieces of ward equipment.

Wards.—It is not advisable to have large wards, possibly 12 beds should be the maximum and this number should be sub-divided by screens into spaces accommodating from two to four beds. Every children's hospital should have a separate building for contagious diseases. This may not be feasible in a very small hospital and in that case it may be necessary to place an isolation suite in a corner or

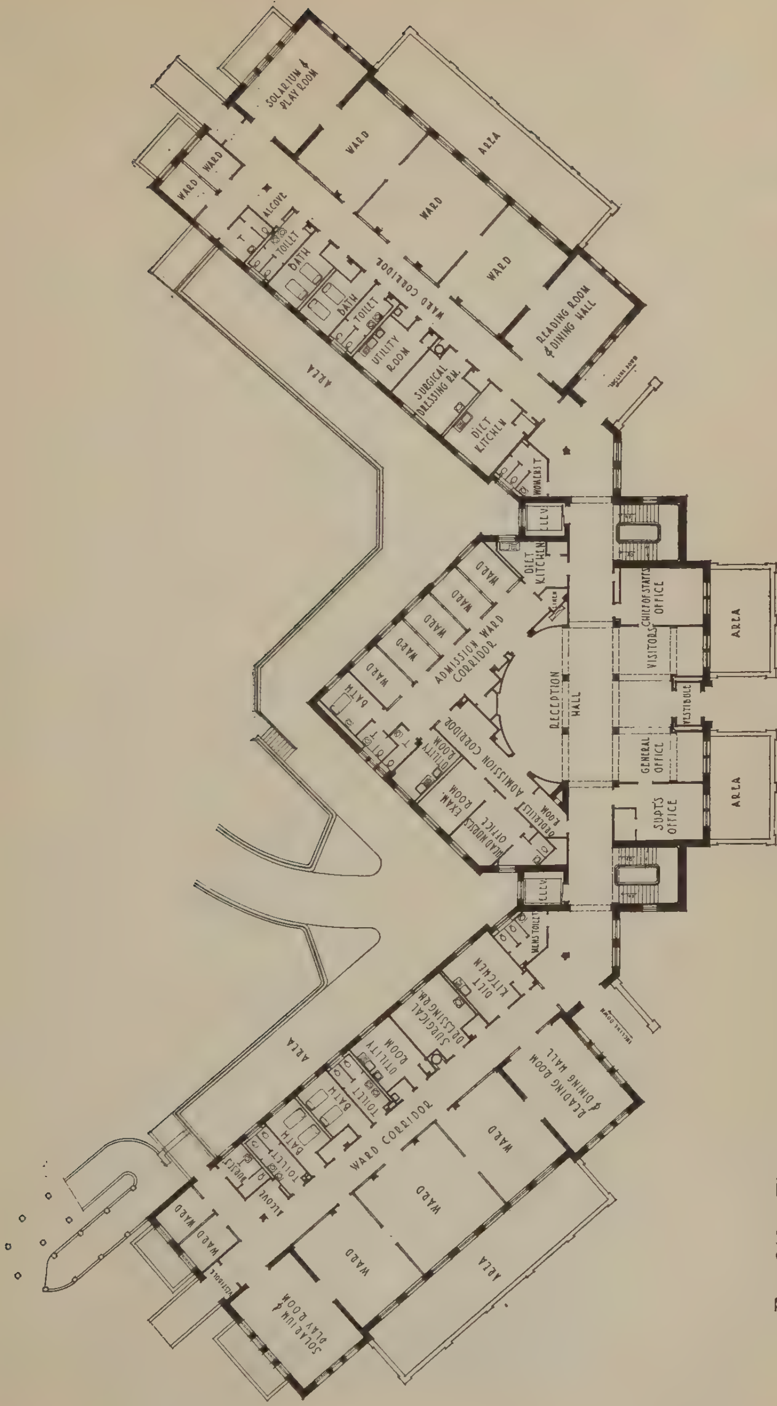


FIG. 219.—First floor, Projected Shriner's Hospital for Crippled Children, St. Louis, Mo. (Wm. B. Ittner, architect.)

wing, preferably on the ground floor, where access to it can be had from the exterior, thereby affording complete isolation. Obviously, such a building or section requires several auxiliary rooms similar to those in the principal building. The illustration of a small isolation building is sufficient to indicate the requirements and it is unnecessary to again describe the arrangement or equipment. The standard sizes of children's beds are as follows:

Children's beds, cribs, basinettes:

Beds.— Typical, 2 ft. 6 in. by 5 ft. 6 in. and up to adult size 3 ft. 0 in by 6 ft. 8 in.

Cribs.— 2 ft. 0 in by 3 ft. 8 in., 2 ft. 5 in. by 4 ft. 6 in., 2 ft. 6 in. by 5 ft. 0 in., 2 ft. 6 in. by 5 ft. 6 in., 3 ft. 0 in. by 5 ft. 0 in., 3 ft. 0 in. by 5 ft. 6 in., 3 ft. 0 in by 6 ft. 0 in.

Popular size for hospitals and homes
2 ft. 6 in. by 5 ft. 6 in.
2 ft. 6 in. by 4 ft. 6 in.

Basinettes.—19 in. by 39 in., 24 in. by 44 in.
30 in. by 15 in. by 15 in. deep
32 in. by 19½ in.by 15 in. deep
24 in. by 14 in. by 8 in. deep
18 in. by 31 in. by 12 in. or 18 in. deep

Proper isolation requires an area of about 70 sq. ft. per bed and a minimum cubic space of about 800 ft. The glass area of windows should not be less than 10 per cent. of the area of the room; the window sills should not be too high so as not to obstruct the view of surroundings too much. The heads or tops of windows should be close to the ceiling to facilitate natural ventilation. Hot-water heating and vapor or vacuum steam heating are preferable to other systems and in every instance the radiators should be suspended from the walls to facilitate cleaning and enclosed by wire screens to prevent burning.

The windows should be arranged to permit ventilation by natural means without drafts. This can be done by windows of the types described later. Numerous ceiling and wall fans should be installed to circulate the air at times when there is not sufficient movement of the outer air.

The cost of installing and operating a system of mechanical air cleansing and ventilation of adequate capacity, is so high that but few institutions will attempt it, as it is questionable if the results are any better with the best mechanical installation than can be obtained by natural methods in localities free from smoke and dust. However, it would be desirable to arrange at least a few special rooms for the highest type of mechanical ventilation, which would permit of holding a temperature at pre-determined points, either comparatively warm in winter or at fairly cool temperatures in the hottest weather. Special provisions must be made in the insulation of walls, floors, windows and doors of such rooms, similar to requirements for cooling and refrigerating rooms.

Signal Systems.—Signal systems for patients' use, such as now generally placed in hospitals for adults are unnecessary in a children's hospital. However, signal buttons should be provided in every room at a sufficient height from the floor to make them inaccessible to patients for the nurses' use in emergencies. These buttons should be connected with lights and other appropriate signalling devices to the supervisory nurse's station, offices and other places where attendants are stationed or congregate.

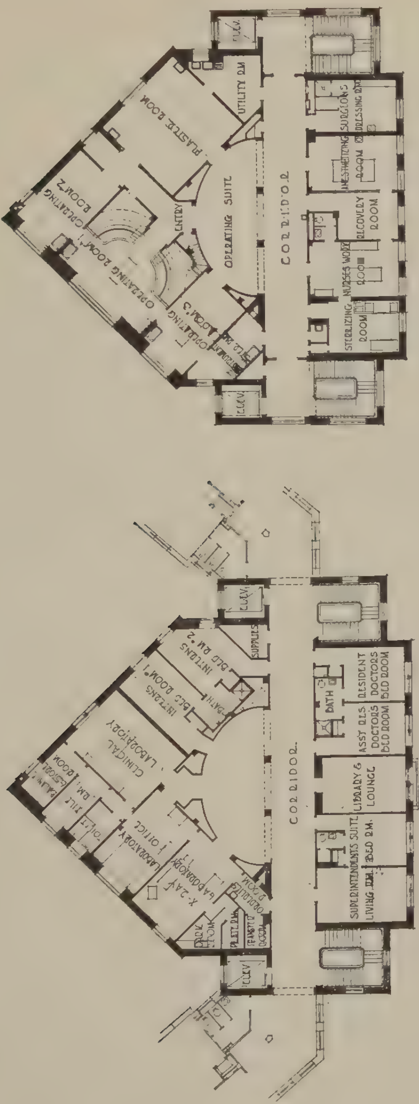


FIG. 220.—Second and third floors, Projected Shriner's Hospital for Crippled Children, St. Louis, Mo. (Wm. B. Ittner, architect.)

Decoration.—Color apparently has as much value in children's hospitals as in those for adults and decorations are helpful in quieting restless children. High colors are obviously out of place. Pleasing tints are available and should be carefully selected to preserve a harmony of the whole.

Simple stenciled conventionalized ornaments of leaves, fruit or animals as used in nurseries provide a pleasing addition to the otherwise barren detail of the walls. These stencils can be placed at the top of the wainscoting and around openings and serve the further purpose of providing a line for changing color and more frequent painting of the wainscoting than of the upper part of walls.

In addition to the line stencils, pictures of mother goose or similar subjects, painted on the walls or on canvas pasted to the walls, or colored tiles set flush in the walls are interesting to children and help to induce quiet and restfulness.

The plumbing fixtures, facilities for bathing, etc. must be quite different from those required for a hospital for adults and will be described later.

Private Rooms.—Private rooms are not as much of a necessity in children's hospitals as in a hospital for adults, inasmuch as children are happier when with others, but a demand for them requires that a number are provided. Usually these should be large enough to also accommodate the child's mother and as the space is limited by walls, not by screens, the area must be considerably more per bed than in a ward, and any room smaller than 9 by 14 ft. will probably be found insufficient to acommodate the required furniture and provide sufficient air space. Heating, ventilating, lighting, signal system and decoration can be similar to that in the wards.

French windows of bed width leading to a balcony are desirable and private rooms should have a private toilet and lavatory adjoining.

Quiet Rooms.—Private or quiet rooms should be arranged in conjunction with every ward for the use of very sick children. The corridor walls should be glazed to permit observation by the nurse without entering the room.

Reception Rooms.—Reception rooms should be arranged for pay and for ward patients, each with special exits. They should be be so connected with examination and dressing rooms that the children can leave the building or be conducted into the hospital without passing through the reception rooms again. The reception room should also be connected with isolation rooms, having separate exits to be exterior for the temporary care of contagious cases which cannot be retained in the hospital and must be taken to another institution. These rooms must also have toilet facilities and arrangements for serving meals. Such an arrangement is shown in the plans of the Sarah Morris Hospital for Children, (Figs. 121–126).

Auxiliary Rooms.—Business offices, physicians locker rooms, consultation rooms, record room, library, kitchens and auxiliary rooms, diet kitchens, floor pantries, utility rooms, sewing room, linen rooms, janitor's closets, laundries, operating department, surgical dressing rooms, plaster rooms, eye, ear, nose, throat and dentistry and special requirements for orthopedics, morgue, autopsy, museum, *x*-ray rooms, laboratories, shops, hydroelectro and physio-therapy, education rooms, nurses' lecture room, house physicians, internes, nurses and helps housing will be much like that of the hospital for adults.

Milk kitchens, couveuse, porches, play room and wet nurses' housing are special rooms requiring special arrangement and equipment.

Wet Nurses.—Pleasant rooms should be provided for the wet nurses with the usual accommodations of a dwelling, such as a living room, dining room, bed rooms, bath rooms and a porch to keep the nurses in a pleasant frame of mind. Their children should sleep in separate quarters. This separation of sleeping rooms and day rooms will prove beneficial, otherwise it will be difficult to have the wet nurses do ordinary house work, maintain a neat appearance and keep their rooms in good order and work diligently. A room should be provided for wet nurses to nurse children without interference, under control and responsibility.

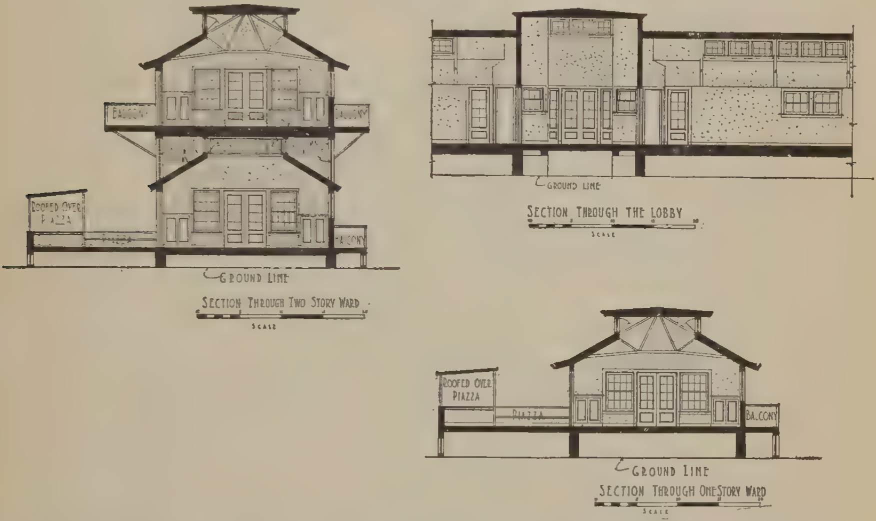


FIG. 221.—Porches and wards, Children's Hospital, Boston, Mass. (Shepley, Rutan and Coolidge, architects.)

It is advisable to have the entrance and exits under the observation of the management.

Porches.—It seems preferable to have an enclosed porch or solarium in direct connection with each ward rather than a general play room. Such a solarium, if divided from the ward by glazed doors and windows will faciliate observation by the nurse of the ward, whereas if the children are sent to a distant play room that would be impossible. The solarium can also serve as a dining room for the convalescent children. The necessity of proper window guards is obvious.

Every ward, including single bed wards should have windows and porches wide enough to roll beds on to them to give the children the benefit of air and sunlight.

Paved, awninged and screened terraces should adjoin ground floor wards, with runways to a garden and their preference over porches of upper stories seems an excellent reason for building low buildings wherever location and ground area will permit.

The arrangement of piazzas of the Children's Hospital of Boston (Figs. 221, 222) is unusual and admirable. It consists of large sliding doors in the south walls of wards with metal plates attached to the doors fitting tightly into a deep slot in the bottom and sides to secure a tight fit. These doors make practically an open ward in summer and allow the beds to be easily pushed out on the piazza to the south, which is 15 ft. wide. There is a narrow roof on the outside of the piazza away from the building, which protects the patients from the direct rays of sun and rain and yet allows sunlight to enter the ward.

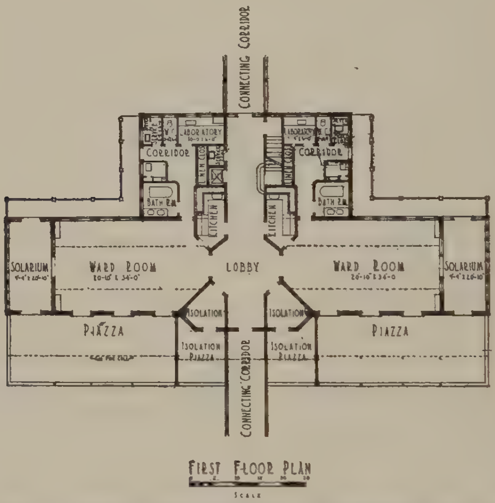


Fig. 222.—First floor, two-story ward building, Children's Hospital, Boston, Mass. (Shepley, Rutan and Coolidge, architects.)

Roof Wards.—A complete roof ward unit with every facility for the care of the patients is very desirable in a hospital located in congested city areas. The walls of such a ward should be almost wholly of sash and glass, thereby providing almost an open air pavilion for very sick children. Every auxiliary, such as elevator and dumb waiter connection, floor pantry, duty room, linen room, etc., should be built.

Roof Gardens.—A roof, play room and yard similarly arranged would also be useful in a hospital of this kind. The roof should be properly paved, enclosed by high strong wire or iron guards, artificially illuminated and set with iron posts and runners for rolling awnings. Space so arranged will be very useful and beneficial in the location mentioned, to convalescent, ambulatory and bed cases. Apparently the children will be under closer observation and more desirably safeguarded and under better conditions than in a yard on the ground.

Lecture Rooms.—Lecture halls and clinics should have separate entrances for students and patients, two entrances for patients; one of these for children with communicable diseases. Preparation rooms auxiliary to the lecture halls should be provided for the children.

Photograph Gallery.—A roomy atelier with the usual dark developing room for photographic work is of great value in adding to the world's stock of scientific medical knowledge.

Materials and Constructions.—Inasmuch as hospital boards are usually inexperienced in the great variety of details of material, finish and equipment suitable for a children's hospital, it seems desirable to direct attention to the newest and best, and not attempt to describe those which are common to all kinds of buildings and which can be safely left to the judgment of the architect.

Manifestly the description of construction will be limited to the permanent fire safe forms of building and not to temporary non-fire resisting forms, such as were used in our Army's temporary hospitals, in which wood was used for construction and enclosure, floors, lathing, stairs and many other parts.

One-story Hospitals.—For hospitals of one-story, of which the floor is practically on the ground level, fireproof construction may not seem as necessary as for a many-storied building. If a portion of the building is two stories high, the second floor should be of fireproof construction, the roof may be of wood construction, provided that the second floor has large balconies on all sides connected with roofs and corridors of other sections of the building. In this manner the shells of ward buildings can be kept as inexpensive as possible, so that future changes will not be hampered by too expensive permanent construction. However, in general, it is assumed as axiomatic that a children's hospital should be of the most approved modern fire resisting construction; no half-way measures, such as attempted fireproofing of combustible material should be considered.

Fire Resisting.—Walls, floors, partitions, ceilings, stairs, floor surfaces, shafts as well as every supporting or structural member should be of incombustible material, such buildings are not only fire resisting but also vermin resisting.

Wood is used only very sparingly, for the fastening of window frames, sash, door frames, doors, cabinets, and equipment; some of these should be of metal and all of them can, if the additional cost is not prohibitive, but it is not essential to have metal doors and windows throughout to provide a fire resisting building.

The aim should be to confine a fire to the room in which it originates, without injury to the remainder of the building and its occupants. There are many instances where fires have completely consumed the contents of a room without passing through a wooden door or to adjoining rooms.

No wood should be used in the construction of supporting members or actual construction of the building.

Types of Constructions.—The choice of type of construction, whether wall bearing, *i.e.*, where the floors and roofs are supported by the walls, or a skeleton construction, in which the weight of building, including the floors and roofs are supported by columns, and the walls are only curtains serving as an enclosure, and not to support loads, depends largely on the area and height of the building.

Fireproof framing and construction consists today of two types; first, steel columns, girders and beams, with a filling of concrete or hollow tile between the floor and roof beams, and, secondly, similar structural members of reinforced concrete.

If the building is six or seven stories or more in height, the building of a full skeleton or frame of either steel or reinforced concrete is advisable for it will permit of the most economical use of a construction plant.

The rental of the hoisting engine, and derricks and the continuous employment of steel erectors is obviously more economical than employing them intermittently floor by floor and employing and discharging masons to build the walls story by story for a wall-bearing form of construction.

If the structure covers a considerable area, notwithstanding that it may have a few stories, one type may be almost as economical as the other for then the walls are about of the same thickness in a skeleton construction as they are for a wall-bearing building, and the building plant and crews of masons and iron setters can be employed continuously by beginning the erection of the frame at one end of the building in each story and constructing it to the other end, and following these with the mason work so that the first end will be ready for the iron setters or form builders when they have completed the work up to the other end.

In high buildings, the thickness of the walls increases their weight and cost to such an extent that a full frame or skeleton is more economic than the wall-bearing type. The various forms of construction will be described later.

Steel construction requires a filling of hollow tile or concrete between beams of the floors and the roof.

Hollow tile generally provides a flat surface for plastering, the ceiling and requires a filling of some kind of concrete on the upper surface to furnish a flat surface for the floor finish to reduce the amount of material required for the floors to a minimum. Concrete filling between beams generally requires a suspended ceiling to provide a flat ceiling surface to receive the plaster.

Since wood flooring has most generally been supplanted by other forms of surfacing in hospitals, hollow tile filling between beams has been found more expensive than reinforced concrete.

Reinforced concrete construction either wall-bearing concrete frame or skeleton type, is generally considerably more economical than steel framing. The amount of steel is much less, the concrete is load carrying or structural and not an inert filling. The number of operations or different parts employed are fewer, and it can be molded to any form without extensive shop work.

Reinforced concrete foundations are always cheaper than the older forms of stone foundations on clay, sand, gravel or mixtures of these.

In buildings in which the loads are supported on the exterior walls, it also seems advisable to build interior supporting walls where the spans between the exterior walls require interior supports in as much as interior columns and girders will be of greater thickness than non-supporting partitions, and in such cases, the columns and girders spaced at equal intervals, for reasons of economy, do not always permit of placing doors at the most advantageous locations. The columns also project into the rooms and present additional projections which are not always sightly and increase the cost of plastering.

There are many forms of reinforced concrete floor construction, some of which are more advantageous than others, depending upon the plan and materials available in the market.

The amount of carpenter work required to build wood forms largely governs the cost per square foot. Simple flat forms are obviously the cheapest in themselves and are suitable for flat slab concrete construction, which provides both the ceiling and floor surfaces, if the spans are short and the carrying requirement low, which is usually the case in a hospital, it is also the cheapest type if sound deadening is not taken into consideration.

If the spans of this form of construction exceed about 13 or 14 ft., the amount of steel and concrete required exceeds that in a ribbed or joist construction, especially where steel forms can be rented. Such forms are held for renting purposes in many places at reasonable rentals.

A combination of concrete joists spaced 4 or 5 ft. apart with thin slabs between them and reinforced in one direction is a fairly cheap form of construction for some uses, without a suspended ceiling, but present the appearance of a beamed ceiling, which increases the cost of plastering and detracts from the appearance of rooms in which these beams are not symmetrical with the enclosing partitions.

Rib or joist construction, in which the ribs are 16 or 18 in. apart require suspended ceilings to obtain a flat plastered ceiling. The additional cost of the suspended ceiling does not make the total cost as high as the cost of other types. A flat ceiling surface can also be obtained by using hollow clay tile blocks, or gypsum blocks between the reinforced concrete ribs, and in markets where the cost of these materials is low, such floor systems are a little cheaper than ribbed construction with suspended ceilings, but their sound absorption quality is not as high. In buildings in which there are several rows of interior columns and these can be spaced into square bays, a two-way system of reinforced joist with clay tile fillings or square metal or gypsum domes with or without suspended ceilings, as the system may require, may be found economical and in these, as well as in other forms of construction, girders between columns may be built within the thickness of the construction, without projecting them below the ceiling surfaces.

The so-called flat-slab system of construction which has flat ceiling and floor surfaces is only economical for buildings such as warehouses, which are built to carry heavy live or superimposed loads of 150 lb. per square foot or upwards. They have the further objection of requiring very large projecting concrete capitals on the columns.

Reinforced concrete is especially adaptable and economical for the construction of stairs, elevator pits, cantilever porch floors. It is also cheaper than steel for the construction of steeply pitched roofs.

Metal lumber, which consist of sheet metal bent and riveted together in the form of rolled steel beams is being used to some extent and is light, easy to set in place, but is of such thin material that there is danger of failure by rust, of sound transmission, and the strength cannot be as definitely calculated as that of rolled steel or reinforced concrete. A determination of its strength depends wholly upon empirical standards. Its resistance to lateral forces which may be induced by settlements is negligible. This form of construction is not being used for large or important structures.

Masonry.—Freight rates largely dictate the choice of materials for the masonry of a building. Materials for concrete, such as gravel, crushed stone, or crushed slag and sand can probably be obtained by wagon or truck haul in almost every locality; having this advantage, and also that of being workable into walls without cracks or joints will be generally selected for sub-grade walls.

Well-laid stone sub-grade walls are good, but more expensive. Hard burned or glazed hollow tile blocks are very suitable and economical for the sub-grade walls of low buildings. Their comparatively low crushing strength makes their use prohibitory for high buildings of wall-bearing construction. The air spaces which they contain give them the desirable qualities of heat and moisture insulation. Hard burned brick and more labor is required for brick subgade walls; also special provisions against the ingress of moisture, such as plastering with portland cement and brushing with hot tar or asphalt. The use of brick for such walls should generally be limited to sand and gravel soils. It is very desirableto provide a damp-proofing course of slate or saturated felt at the ground line where the walls of the super-structure begin. Three courses of roofing slate laid in portland cement mortar, or three courses of saturated roofing felt laid in hot tar and projecting over both faces of the wall will stop the capillary attraction of moisture into the walls of the superstructure, which are often stained by moisture where such a measure is not provided.

The nearby industries will also dictate the choice of material for the facing of walls above the surface of the ground; for these, face brick, with or without stone or terra cotta trimmings, common brick, or clay tile finished with cement coating, rubble stone laid in random courses and sizes, or coursed cut stone, and many other varieties can be used at varying costs in proportion to the importance of the building or the available funds.

The facing material can be backed with common brick or hollow tile, or cheap forms of cement blocks. Where irregular pieces of stone are found in mountainous districts they can be used for the construction of rough solid stone walls and finished with a smooth or pebble-dashed cement coating. Ordinary hollow clay tile of the same thickness as the wall has the disadvantage of moisture, condensation on the joints on the interior and also of the passage of water from the exterior through joints formed by shrinkage, and it is not advisable to use hollow clay tile unless the walls are built of more than one thickness which will permit of breaking and covering the joints so that there will be no joints extending from the exterior to the interior. The best results are obtained by mopping both exterior and interior surfaces of the principal course of tile with asphaltum or bituminous compounds, which form a waterproofing and insulation and remain "tacky."

The exterior can then be cement coated and the interior lined with a thin or furring course of hollow clay tile to receive the finishing plaster.

Specially shaped interlocking hollow tiles are obtainable which on account of their form are not subject to condensation, or the passage of moisture, and some of these also have a surface resembling the color and texture of face brick. They are laid with alternating courses about 8″ and 4″ in height and are both economical and of pleasing appearance. The difficulty of obtaining surfacing on cement blocks or artificial stone which does not absorb a high percentage of water, and the objectionable appearance of water-soaked walls for several days after a rainstorm is generally known. Their shape and the difficulties of obtaining a satisfactory surface texture and color is an esthetic objection to their use. They also require special insulation against condensation and joint moisture on the interior.

Pipe Shafts.—It would be very desirable to have all plumbing, heating, and other pipes and conduits in shafts or ducts of such dimensions that they would be immediately accessible to the engineer for repairs if a leak or break occurred. Such an arrangement is practical for the plumbing pipes of a building in which the bath, toilet, serving and other rooms having plumbing fixtures are similarly located on every floor, for in that case a minimum number of shafts will be required, but it is a practical impossibility to provide shafts for the plumbing pipes of almost any modern children's hospital, in which the subdivision of the different floors differs as much as it generally does. The arrangement of the administration, receiving, out-patient, operating and other departments differs so greatly from the patient or ward floors that plumbing fixtures cannot be so located that they will be in shafts of the upper floors or have independent shafts of sufficient dimension to permit of working in them. That could only be done by providing horizontal working or service spaces below every floor at a greatly increased cost of building. If shaft building were carried to a finality it would almost double the cost of the building. Such shafts must be of fire resisting material; they require neatly fitting iron doors and frames, and grating floors to support the mechanic making the repairs. There must be so many rising and return pipes connected to radiators of the heating system that it is impractical to place these in large shafts and they must either be built into a small wall channel covered by plastering, or exposed in the rooms. Exposed pipes require frequent painting. The insulating covering is damaged and must be replaced from time to time and they increase the cost of janitor service. It therefore seems advisable to adopt a middle course, i.e., place pipes in shafts wherever fixtures or rooms of similar function are superimposed and conceal those pipes behind plastering which serve isolated fixtures.

If the proper kind of material is used for piping, if it is properly supported and arranged to permit it to freely expand and contract, there should be no leaks or breaks for many years, and an occasional tearing up of floors or breaking into a wall to repair a leak will cost but a fraction of the capital which must be invested in constructing a complete system of shafts and ducts.

Partitions.—There are many materials or combinations of materials for the construction of interior partitions or subdivisions or non-load supporting walls. Those most generally used are clay tile or gypsum blocks and metal lathing and plastering. Cement blocks are rarely used for this purpose. Clay tile and gypsum blocks are used in thicknesses of 3 in. for partitions 10 to 11 ft. in height and of increasing thicknesses for greater heights. Inasmuch as door frames and doors should be placed in partitions at least 4 or 5 in. in thickness, clay tile and gypsum block partitions are used to a greater extent than other and thinner types. Sheet metal studs or uprights, which are formed to receive and hold paster boards, provide an excellent form of partition. In cases where economy demands a reduction of fire resisting properties wood studs with plaster boards or metal lath can be used. Three-quarter inch or 1 in. steel channels placed 10 or 12 in. apart with woven wire or metal lath secured to them afford a foundation for plaster which is applied on both sides and forms the so-called solid plaster partition, measuring from 1½ in. in thickness for ordinary story heights to greater thicknesses for higher stories. Other solid plaster partitions are built by the use of a fabric consisting of woven wire with burned clay crosses on the intersections. This arrangement provides a surface for plastering on both sides with the use of less steel than other form of solid partitions. Both kinds of solid partitions are extremely rigid, if the thickness is properly proportioned to the height, but their limited thickness presents objectionable features in the installation of electric conduits, switch boxes, and fixture outlet boxes, which is not the case with clay tile, gypsum blocks or other thick partitions.

The limited thickness of solid partitions also makes it impossible to use modern forms of sanitary or flush door trim. Similar materials are used to insulate exterior walls, in temperate and colder zones, above 30 degrees of latitude, also to conceal projections or recesses, to furnish flat or flush wall surfaces. Gypsum blocks are sawed into two slabs of 1½ or 2 in. thickness and clay tile blocks are scored before burning, so that they can be split into two equal parts by a blow with a trowel.

In building partitions and furring, provisions must be made for the fastening of woodwork, plumbing fixtures, cabinets and bath room and toilet fixtures, such as mirrors, towel bars, paper holders, etc. So many different trades are required to construct the building over a considerable interval of time that it is almost impossible to maintain pieces of metal in the partitions in walls for the fastening of such articles. Where it has been tried, it has usually been found necessary to cut the walls to find or relocate the concealed fastenings and incur considerable expense for patching. Small pieces of wood built into the partitions and furring for the fastening of such things do not increase the fire hazard and provide a convenient fastening, the exact location of which need not be predetermined or maintained.

Before plastering is begun walls and partitions must be prepared to receive woodwork by securing strips of wood, known as grounds, to the partitions and other parts.

Plastering.—A strong, hard, smooth plaster surface is everywhere desirable, but the greater cost of such material and increased labor generally requires the use of ordinary lime mortar or patent plaster in the major portion of the building, and to limit the use of hard strong material, which can be troweled to a glazed surface, such as Keen's cement, to the operating department, laboratories, sterilizing rooms and to wainscoting.

It is a practical impossibility to trowel a smooth vertical surface of portland cement and sand. Obviously, this result can be approached on floor work, but not on wall work, with a material which does not set for several hours after being moistened and will continually slough off the wall. Portland cement can be made to adhere to a masonry wall surface by an admixture of lime, which obviously reduces its hardness, and it cannot be troweled to a surface which would be satisfactory in rooms occupied and used by patients unless so large a quantity of lime is added that all practical benefits appear to be lost. If it could be troweled to a surface having a similar texture throughout, there might not be any objection to a rough texture, but portions of it will be smooth, and other portions rough so that it does not present a satisfactory appearance.

Brick, clay tile, gypsum block or plaster board should receive at least one coat of coarse plaster material and one coat of finishing material, such as gypsum or lime putty. A better and truer surface can be obtained by the application of two coats of coarse material and one coat of finishing.

Metal lath must receive at least three coats of plaster material. Concrete must be specially prepared by the application of tacky tarry substances to hold plaster securely. If it is not so prepared, the plaster is likely to fall in the course of a few years.

If steel or sheet metal door trim, metal corners, metal base or mop boards are to be installed, or if terrazzo or artificial marble sanitary bases are to be applied, these should be placed before the plastering is begun.

Suspended ceilings are generally built of metal strips or rods to which woven wire or metal lath or plaster board is secured and then plastered in the same manner as partitions constructed of the same materials. Such ceilings afford the advantage that they can be hung at different depths in different rooms and cover conduits and pipes which must be installed horizontally and which it would be difficult to conceal on top of the floor construction without providing steps into rooms as is frequently done for bath rooms, but which should not be done anywhere and especially not in a hospital.

Ventilating ducts and soil pipes serving batteries of water closets and other fixtures would be generally too unsightly if exposed below a ceiling.

A saving in janitor service on account of coved or rounded corners is negligible, but they soften the lines of rooms which otherwise appear very plain and hard and do not accentuate the slight soiling of walls which air drafts apply only too quickly.

A rounded steel corner and plaster jambs and heads of window openings in combination with a slate or soapstone or other substantial window stool appears to furnish a most desirable finishing for windows. Woodwork increases the first cost, maintenance costs and janitor service.

Sound Proofing.—The almost universal complaint of the ill effects and annoyance of noise especially in hospitals has resulted in the invention of sound deadening, or more properly sound-absorbing materials; one of these a combination of specially made felt, muslin and air spaces will absorb a large percentage of the sound originating in the room in which it is applied; another material is a wall plaster composed of magnesite and a crushed volcanic stone, which does not absorb as much sound as the first, but if applied on the walls above the doors as well as on the ceiling, it will absorb almost as much as the first, if that is applied only on the ceiling. The sound-absorbing qualities of both of these mediums are depreciated by ordinary oil painting and require special treatment for color effects.

These sound-absorbing materials in corridors and rooms in which noises originate, combined with soundproof doors and sound-absorbing floors will improve sound conditions to a surprising extent.

Roofing.—Roofs are rarely accessible to inspection and receive little attention until they develop a leak. It is consequently important that only the most suitable and best materials are used for this important part of the building. Saturated felt, composition and gravel roofs of the best quality are obtainable everywhere and are probably most satisfactory for flat roofs which are not used for solaria or promenades.

The standard specifications of the Barrett Mfg. Co. or the guaranteed specification of groups of manufacturers are available from dealers and should be followed, inasmuch as these manufacturers furnish free expert inspection.

Roofs which are used for solaria or promenades must have a good saturated felt and composition roof as a waterproof foundation, and a wearing surface of clay tile or thick slate laid in a waterproof compound. The ingredients of these compounds must be carefully proportioned to prevent them from oozing or boiling out of the joints in hot weather; otherwise the compound will spread on the tile or slate and adhere to footwear and will be tracked on the floors of the building.

Portland cement concrete about 3 in. in thickness and finished with a troweled cement wearing surface, laid in squares with joints made the full thickness of the concrete and these filled with a waterproofing compound, are sometimes used in place of tile or slate.

The cement of the wearing surface should be darkened with lamp black to reduce annoying light reflection, but this kind of roofing has the disadvantage of weight for the support of which special provisions must be made.

Slate, Tile.—Slate, clay tiles, asbestos shingles, copper and tin are the most suitable and durable for pitched roofs. Tile can be obtained in a variety of forms, such as shingle, interlocking, Spanish, pan tiles, etc.

Various colors and textures are harmonious with different colors of face brick, stone, or cement finish. Asbestos shingles, unless of a special quality, do not have an interest in texture or color and tin must be painted at frequent intervals. Copper and zinc if used for pitched roofs should be formed into long pans laid between wooden strips, spaced about 18 in. apart from eaves to ridges. The wooden strips and the edges of pans should be covered with inverted channels of the same material. Slate, tile and copper, as well as asbestos shingles, should be secured by specially formed copper nails. Ordinary steel nails rust away only too quickly.

Asphalt shingles and other imitations of slate roofs are often torn up by wind storms and are otherwise too transient for durable building construction. Tin, zinc and copper shingles, imitating various types of tile roofing, are uninteresting in color and it is preferable to use these materials in other forms rather than to attempt to imitate another material.

Nailing.—Special provisions must be made on roofs of fireproof construction to secure the roofing material, either by wooden strips buried in concrete, or by applying wood strips at regular intervals for proper nailing. Obviously special provision must be made to fasten these strips permanently. A 1½ or 2 in. course of "Nalecode," a fireproof cementitious material into which nails can be driven, provides a satisfactory nailing surface for slate or tile.

Flashing.—The joining of roofing materials to walls and chimneys, which is termed "flashing" and "counter-flashing," is usually the first to deteriorate unless it is of durable material such as copper. Such material should also be used for the gutters, rainwater conductor pipes, skylights and other roof fittings.

Snow Guards.—In locations subject to heavy snow fall it will be well to provide guards to prevent the slipping or sliding of snow. These guards generally consist of heavy glavanized wire loops projecting above the roof and a pointed end driven into the roof construction and placed at frequent intervals on slate and tile roofs. An iron railing 6 or 8 in. in height on the edge of the gutter is a frequently used expedient over entrances to protect these from miniature avalanches.

Floor Surfacing, Base Boards.—The question of what kind of a floor to select for a hospital is one of the most insistent and important questions. It is obvious that the problem is not identical throughout the hospital. The requirements of a good floor for the operating department, culinary department, the wards and private rooms and the toilets differ greatly; consequently, it will be found that several kinds of flooring should be used in the same building.

On account of the high cost of maintenance and unavoidable shrinkage, the use of wood for wearing surfaces has been generally discontinued. Thoroughly seasoned hard wood, parquetry floors laid in asphaltic compounds on smooth cement floors provide a beautiful, durable but expensive floor.

Portland cement floors cannot be laid with a uniform hardness and finish. Troweling and mixing cannot be done so perfectly that every portion of a floor will have the same proportions and the same amount of troweling, consequently the surface wear varies. It must be laid with joints unless one is willing to risk the danger of irregular cracks.

Plain cement floors are, however, suitable in store rooms and other spaces which are not prominent. The appearance of portland cement floors can be improved by heating them with inverted gasoline torches, filling and polishing the surface with a colored mixture of paraffin and beeswax. Special cement paints are only surface treatments and require constant repainting, especially in doorways and corridors, where they receive the hardest wear.

Chemical hardeners for portland cement wearing surfaces improve their wearing qualities. Asphalt floors are useful in laboratories, but their color is too dark for wards or corridors.

The reaction of patients to pleasing colors is now generally admitted. This arbitrarily rules out all of the flooring materials described here-in-above, except wood. A pleasing color is an important desideratum in almost every part of the hospital.

Mastic flooring, which is a plastic material, is laid on cement floors to a thickness of about ⅛ in. Its color is a dark reddish-brown, green and buff and is quite soft to the tread. It is suitable for laboratories, laundries, and for improving old defective cement floors but the red and green varieties are too dark to be used in wards which should be as bright and cheerful as possible.

Battleship linoleum cemented to portland cement floors furnishes a pleasing wearing surface but requires careful janitor service, polishing at intervals and will usually shrink, and have excessively large joints if laid in wide widths. This fault can be partially, if not wholly, prevented by cementing one or two courses of heavy felt paper to the foundation cement and cementing the linoleum to the felt.

Magnesia composition, known by various trade names, such as "Asbestone," "Flexolite," "Monolith," Marbleoid," etc., also requires a smooth portland cement foundation and is laid in thicknesses of about 7⁄16 in. It can be obtained in a variety of colors and is also laid in a plastic state and can be applied to walls to form sanitary coved bases, or mop boards, which cannot be done with mastic.

Granite or marble chips are sometimes mixed with it and machine grinding exposes the marble or granite so that its appearance resembles terrazzo. This material can also be made mottled in two colors, which has the advantage of concealing footsteps which are very often very prominent on newly washed linoleum, magnesia or other monotone floors.

Well-seasoned linoleum cut into pieces approximately 24 in. square and cemented to a smooth portland cement foundation with joints about 3⁄4 in. in width and these filled with black, buff or red magnesia, combined with sanitary coves and borders formed of magnesia, furnishes a very attractive, durable and resilient flooring.

On account of its pleasing appearance and comparatively low cost, terrazzo which is laid about 2 in. in thickness on almost any subconstruction has found great favor in recent years. The lower 1½ in. of its thickness consist of portland cement, sand and crushed stone and the upper ½ in., or wearing surface, of colored or uncolored portland cement and crushed marble chips of one or different kinds of marble. It is also an excellent material for sanitary bases. It must be laid in squares of about 6 by 6 ft. or less with joints extending through the material to the foundation to compensate its shrinkage, otherwise it will crack into irregularly shaped sections. These joints are usually marked by laying rows of 3⁄4 in. squares or tesseræ of marble along each joint, also in border lines around the rooms.

Grooved strips of wood with a band of sheet brass inserted on edge in the groove and placed at regular intervals to divide terrazzo into squares have recently been placed on the market and provide a very efficient method of forming full joints and improving their appearance. After the terrazzo has set it is ground to a true smooth surface by electric grinding machines and well polished by hand stones. Specially formed grinding stones are used for sanitary bases of all forms.

There are many other types of floors which may be used for special functions but are generally not used in large areas on account of their greater cost. These are marble and ceramic mosaic, artificial marble or terrazzo tiles, cement tiles, natural marble and stone. The use of these is generally confined to entrances and reception halls. Ceramic encaustic and flint tiles, also 3⁄4 in. and 1 in. squares, hexagons and circles which the makers paste on sheets of paper to facilitate laying are esteemed for their impermeability and are generally used in kitchens, operating departments, dressing rooms, sterilizing rooms and utility rooms; 6 by 6 in. or 9 by 9 in. quarry tiles, either red, brown or black, are often used in culinary departments, porches and solaria on account of their strength and coloring.

Cork tile is an excellent material for many places where it does not receive too hard usage. Its pleasing variety of color, resilience and noiselessness make it especially desirable for ward rooms, corridor runners, conference rooms, offices and lobbies. Rubber tiles, in the form of inset mats, should be placed in front of elevator doors to reduce the danger of a person slipping and falling. There is a new marbleized rubber tile on the market which is made of almost pure new rubber and its appearance so attractive that it is useful in entrances, reception rooms, corridors and other locations where noiselessness and appearance are the principal factors.

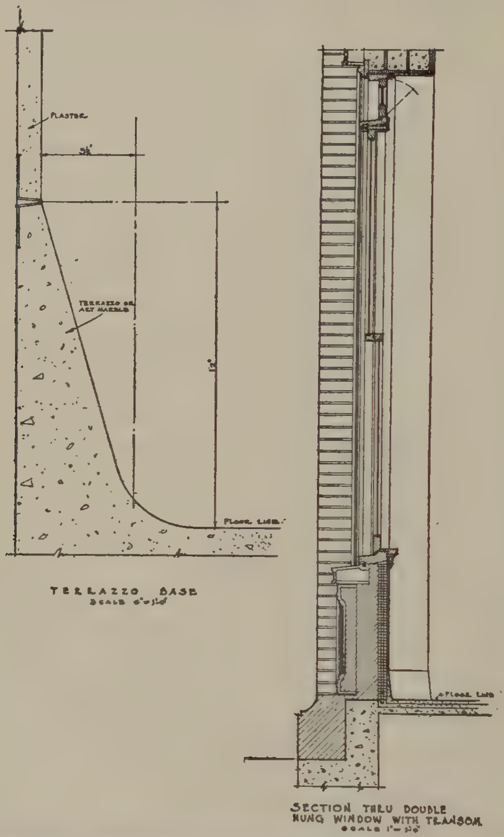


Fig. 223.—Terrazzo base and transom ventilator. The sloping baseboard protects walls from the impact of wheel chairs, stretcher carts and other vehicles. The small transom is an efficient ventilator.

Tile known by the trade names "Linotile" and "Beavertile" are special linoleum compositions of an excellent quality; they are made in a variety of sizes and colors. Resilient and sound absorptive, they are very useful in places similar to those recommended for cork and rubber.

There are several tiles on the market which are apparently smooth, but are almost slip-proof. They are especially useful around moving machinery, inasmuch as oil does not appear to affect their non-slipping quality, also on stairs, near elevators, and on ramps or sloping runways. Alumdum tile is one of these. Others of a different composition contain abrasive substances.

Terrazzo or tile should be used in elevator cabs in lieu of linoleum, rubber, or cork, which does not withstand the very hard usage to which an elevator floor is subjected.

Base boards must be of durable material, inasmuch as they receive very hard wear and should be of sanitary coved form and the upper portion flush with the plaster to reduce janitor service. The joint of these two materials should be striped with oil paint.

Considering maintenance and first cost, magnesia cement and terrazzo are the most useful, and inasmuch as it is not possible to give many of the flooring materials a proper form, terrazzo is being generally used for bases and borders, notwithstanding that the field may be linoleum, mastic, ceramic tile, rubber or cork.

The bases in children's hospitals should be high, sloped from the top to a point on the floor about 3 in. from the walls to protect these from wheel chairs, go-carts, velocipedes, etc. This detail is illustrated in Fig. 223.

Wainscoting.—The constant painting required to maintain walls in good condition is a considerable portion of hospital maintenance cost. The lower or wainscoting portion suffers especially and requires washing and painting more often than the upper portion of the walls, and the number of paintings of the latter portion can be reduced by painting a line 5 or 6 ft. above the floor, which will permit of washing the lower portion without affecting the upper portion and similarly the lower portion can be painted. The hard barren appearance of wards and corridors can be improved by a small colored stencil placed on the dividing line, and if harmonious colors are used for the line and stencil, and these are carried around doors and other wall openings, the appearance is improved still more.

Plastered walls suffer so much from the impact of furniture and other articles, especially in corridors, that it is very desirable to wainscot these with a strong hard material having an integral coloring which requires only occasional washing and not repainting, but the difference in cost of plaster and several coats of paint and a durable material is so considerable that few hospitals can afford to make use of them.

Brown glazed brick of ordinary shape are quite economical if laid in brick walls where they are a substitute for one course of common brick. This usually occurs only in basements, possibly in kitchens; It would not be practical to line clay tile or gypsum partitions with material fully 4 in. in thickness. For such cases it is possible to obtain soft glazed brown or buff bricks 4 by 8 by 1 in. in thickness which can be laid flat against the tile and will project less than 1 in. beyond the surface or the plaster above the wainscoting, forming a dust gathering ledge, but this is the case with almost all wainscotings of durable materials. Brick glazed with a white, cream or speckled porcelain glazing, and also make in dark colors, can be used similarly but the cost is greater. In addition to these there are the usual glazed tiles of various shapes and sizes, marble, slate, soapstone, white glass, terrazzo and artificial marble. Obviously, a material which can be obtained in large pieces will have few joints to keep in repair and is consequently preferable to tile of which from 4 to 25 pieces are required for each square foot. The joining material can never be made as hard or smooth as the wainscoting material, consequently it absorbs water and is grimy in a comparatively short time.

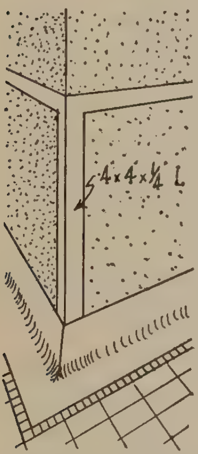


Fig. 224.—Angle iron corner and stretcher cart protectors of walls.

White glass is the most impervious, and can be obtained in large pieces but must be used in thin pieces to be obtainable at a reasonable expense. If the edges are cut in the ordinary manner they soon have a dirty appearance; if the edges are ground smoothly to fit close together and not to hold dirt they improve the appearance greatly but increase the cost proportionately.

Thick polished white or cream colored glass is known as Carrarra glass and thin rolled glass, which has a wavy surface, is known as Opalite. Partitions for toilet room stalls can be made of Opalite by cementing several thicknesses together, grinding and polishing the edges where these are exposed.

Wall Protection.—Strong pieces of iron of angle shape (Fig. 224) about 3/16 in. in thickness lapping about 4 or 5 in. on each side of corners and doors should be placed in corridors and other places where there is considerable travel. The corners should be bent round and these protection angles anchored into the tile or masonry walls prior to plastering and at such distances from the rough walls that the finished plaster will be flush with their surfaces. The height should be about 4 ft. It is also advisable to place flat iron strips of such metal flush with the plasters about 14 or 15 and 36 in. from the floor to protect the walls from chairs, go-carts, operating and food carts. In very narrow corridors, it is advisable to place iron pipes supported on brackets at such a height from the floor and distance from the plaster that they will protect the walls.

Plinths or bases of the same form and materials as the sanitary bases should be built under all woodwork, such as door frames, casings, cabinets and other fixtures so that scrubbing and scrub water will not damage the woodwork.

Stairs.—Woodwork should not be used for the construction of finished surfaces of stairways other than for hand rails. Stairs should be built of durable impervious material which does not require painting. The ordinary form of incombustible stairways in which the strings and risers are of cast iron require constant attention to keep them in good appearance by painting and scrubbing. Iron treads require more similar maintenance and are noisy.

Terrazzo stairs, of which the entire stairway except the railing is built monolithically, are most satisfactory in appearance and use.

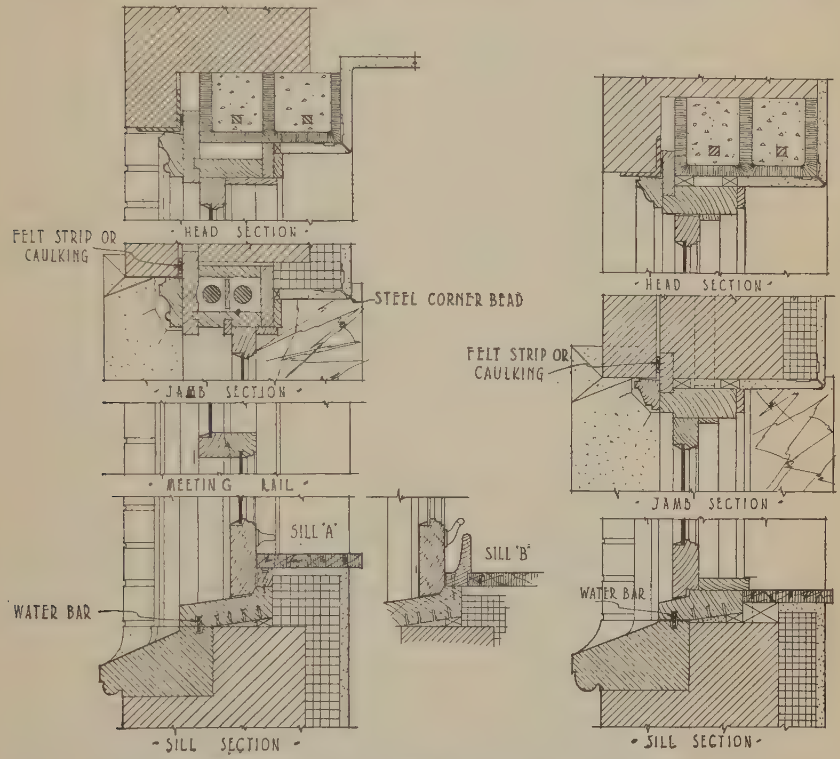


Fig. 225.—Detail sections of a standard box frame, double balanced sash window adapted for hospital use, and detail sections of a casement sash swinging outwards. Sill "A" is designed to open the meeting rail without opening the window at the sill and sill "B" has a permanent draft deflector. Note the sill water bars, felt caulking strips, steel corners, plastered jambs and absence of casings on the inside of the wall.

The strings can be joined to the sanitary bases on the floors around the landings and all angles can be rounded to produce the sanitary cove throughout their extent. The stairways which are used constantly between the lower floors may be made safer by the introduction of a safety tread nosing, of which there are various kinds, *viz.*, abrasive metal lead and steel, or lead and brass, and alumdum tile. In children's hospitals it is a measure of safety to build the stairs without landing or stairway balustrades. This can be accomplished by building a wall in the well, extending from the bottom of the stairs to the ceiling of the uppermost story to which they lead. Such a wall will also form a support for the stairway and hand rails.

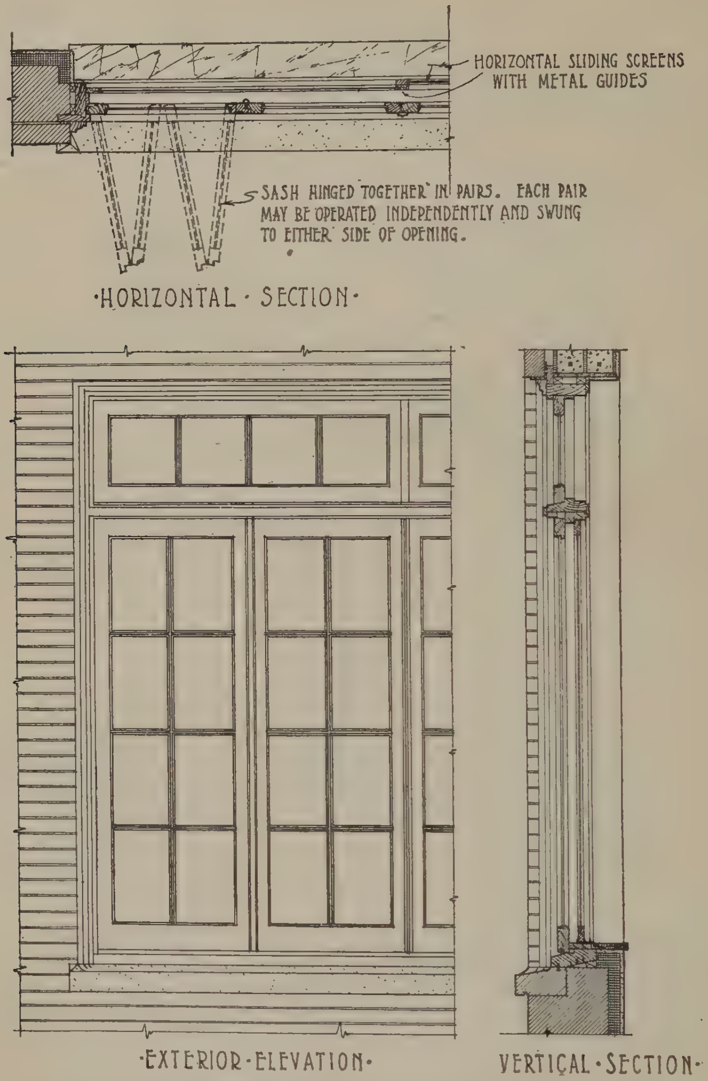

HORIZONTAL SLIDING SCREENS WITH METAL GUIDES
SASH HINGED TOGETHER IN PAIRS. EACH PAIR MAY BE OPERATED INDEPENDENTLY AND SWUNG TO EITHER SIDE OF OPENING.
·HORIZONTAL · SECTION·
·EXTERIOR·ELEVATION·
VERTICAL·SECTION·

Fig. 226.—The Whitney casement sash. The sash can be pushed to one side of the largest window opening, providing almost 100 per cent. open area.

A reinforced concrete inclined slab built to the slope or rake of the stairs provides an economical support.

Windows.—The windows are obviously one of the most important elements of a building and much thought has been given by designers and manufacturers to produce new and more convenient types than the ordinary American double-hung window (Fig. 226) which furnishes only one-half of the full opening of the window for ventilation.

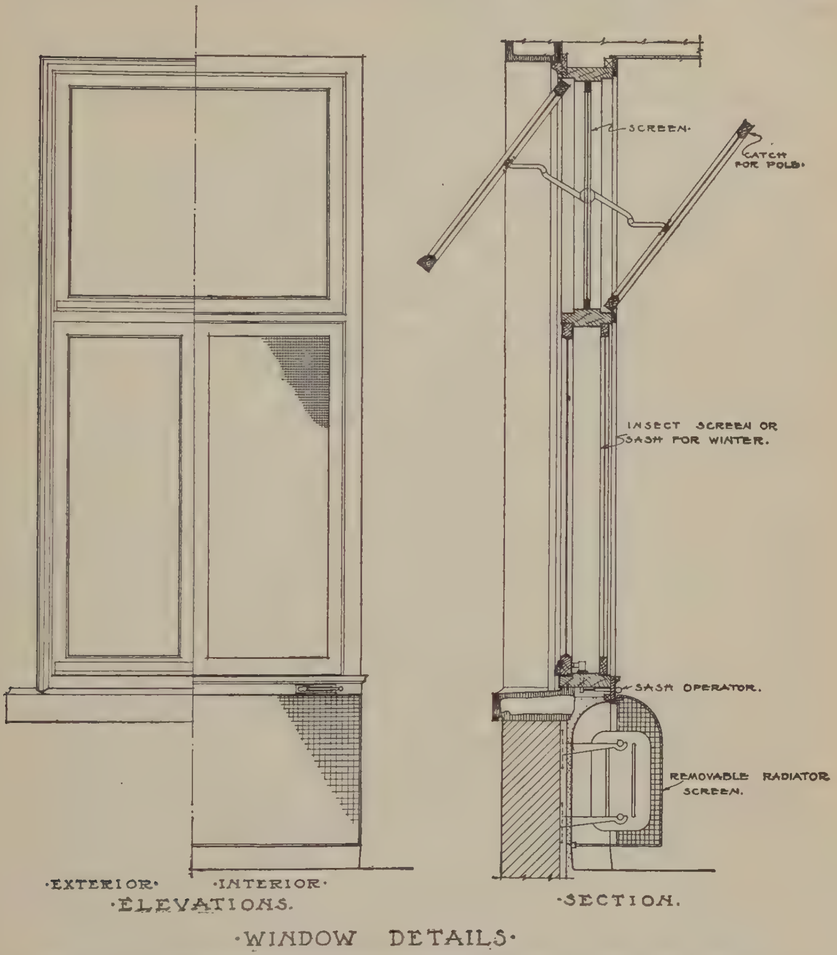


Fig. 227.—Casement and transom window of Sarah Morris Hospital for Children, and Grant Hospital, Chicago. Lower sashes swing outwards and are operated by casement sash adjusters, the screens are hinged on the inside. An inward pull at the top of the inner transom sash by means of a window pole opens the outer transom sash which serves as a protection against rain, the inner sash deflects air currents towards the ceiling. The transom screen is stationary and mortised over the two arms at their pivot. The whole area of the window is available, transforming many rooms into an open air ward.

Casement or hinged windows (Fig. 225) opening inwards or outwards have been tried. Both forms have advantages and objections. Those opening outwards require special forms of hardware to hold them rigidly against the effects of wind, but it seems impossible to make these fittings sufficiently strong or simple in operation to make them satisfactory in a building in which the turn-over of employes is frequent. There are many patented arrangements of double-hung sash which permit of dropping both sash inwards to obtain the full area of the opening for ventilation and to make cleaning convenient and safe.

The Whitney window (Fig. 226) is an arrangement of sash extending from the sill to the head, which fold in such a manner that the entire sash can be pushed to one side for the full area of the opening. These, however, require the screens to be placed on the inside and opened each time that the sash are opened or closed.

Inasmuch as ventilation from the top of a window is the most efficient and is less likely to produce objectionable drafts, double-hung windows with transoms are considered advantageous. Such transoms require transom lifts which are sometimes difficult to operate and the use of friction hinges which will hold the sash at any position is a better arrangement. A combination of two transoms, the inner one of which is hinged at the bottom and the outer one at the top, the two connected by a pivoted link which will cause the bottom of the outer sash to move outwards when the upper edge of the inner sash is pulled inwards is an improved arrangement which protects the opening from rainstorms and undue drafts (Fig. 227).

Small transoms only for ventilation, not for light, are useful if properly arranged with insect screens and baffle boards or louvres which will prevent the ingress of snow and rain. Figure 223 illustrates such an arrangement used in the Chicago Lying-in Hospital. This device allows a continuous exchange of air, which is not noticeable as a draft. An arrangement of a specially high bottom rail as shown in Fig. 225 provides another small opening in the middle of double-hung windows, which serves a similar purpose.

There are also several types of patented ventilating boxes and sloping pieces of glass to place under the bottom of the lower sash.

Figure 225 illustrates a wooden arrangement for a bottom ventilator.

The combined use of small openings at the top, bottom and middle of a double-hung sash window furnishes an excellent arrangement for window ventilation, and if these windows could be opened for the full opening of the frame on the hottest days, a combination of this kind would seem to be the ideal window.

There are a number of patented windows, usually used in factories and office buildings, which may be adapted for hospital use. These have two or more sash in height, equipped with special metal pivots and arms or pulleys and cords, making it possible to swing the upper portion of each sash inwards and thereby obtain practically the entire frame opening. Pivoted sash factory windows, having any number of sash in height and opened and closed simultaneously by chains, have been used in hospitals in the tropics, but these windows are usually made of steel. It would seem very adaptable, however, for solaria.

There is also the reversible double-hung sash window of which the sash are counterbalanced and can be raised and lowered as in the ordinary window, also swung inwards from the top by releasing hinged stops on the frames.

The Lunken window is made complete in the factory and delivered glazed and screened to the building. It has a box over the top of the frame, in which both glazed sash can be slid, thus opening the entire window for ventilation. It also is equipped with overhead pockets for screens, which can be raised into the pockets during winter months and consequently save the cost of removing, resetting, and storage space. A small flap at the bottom of both pockets closes the opening and the appearance of the window in the finished building does not differ from the oridnary double-hung window.

Steel frames and sash have a very neat appearance. Such windows are made to close accurately and weatherproof. However, the material, expert labor, and special hardware make their cost much greater than wood frames or sash.

Guards.—Removable metal window guards to prevent children from falling out of windows are on the market. One of these is a disappearing grille which can be collapsed and folded into a side pocket.

Another can be removed by a special releasing device and such a one can be used in any number of windows without providing one for every window if these are equipped with an appropriate catch.

Shades, Blinds.—The fitting of roller shades is a difficulty encountered with the use of almost all of the special types of windows and their selection requires very careful consideration of this feature. Shades must be fastened to hinged and swinging sash and are a continuous source of trouble if fastened to a window frame in the manner customary where ordinary double-hung sash windows are used. It seem almost necessary to use some form of Venetian blind or patented shades for such windows, but there is again a difficulty when using casement sash swinging inwards. A patented form of shade is made of a heavy specially woven pongee colored cotton goods pleated horizontally with eyelets at the ends strung over a strong steel wire, fastened to the top and bottom of the window. These shades can be raised from the bottom or lowered from the top and are held securely against the wind in many positions. They are very durably made and can be cleaned many times.

Dust Screens.—The common form of muslin or cheese cloth dust screen secured to a wooden frame and placed under the bottom sash of a window has been greatly improved by the introduction of a patented article in the form of bolting cloth secured to a metal Hartshorn roller which will unwind or wind up the cloth by raising and lowering the sash. The cloth is secured to the roller by a slat and this to the sill of the frame by turn buckles to make it easily removable for washing. The sides are engaged by metal wings to provide a tight joint on all sides.

Stop Screws.—There are many little devices which improve the care and use of windows; among these are adjustable stops held in place by screws set in slots with special washers which permit of adjusting the stops to a snug fit after the woodwork has dried out.

Water Bars, Wind Stops.—A metal bar (Fig. 225) set in cement to remain in a groove in the stone window sill and into putty in another groove on the underside of the wood frame will form an absolute stop against the ingress of water or wind in this part of the frame, and strips of tin nailed to the front faces of the frames before the brick work is laid will form a tight joint at the sides, if it projects into the mortar between the courses of brick. A narrow strip of felt (Fig. 225) tacked to the face of the frame on the sides and top is also a good device.

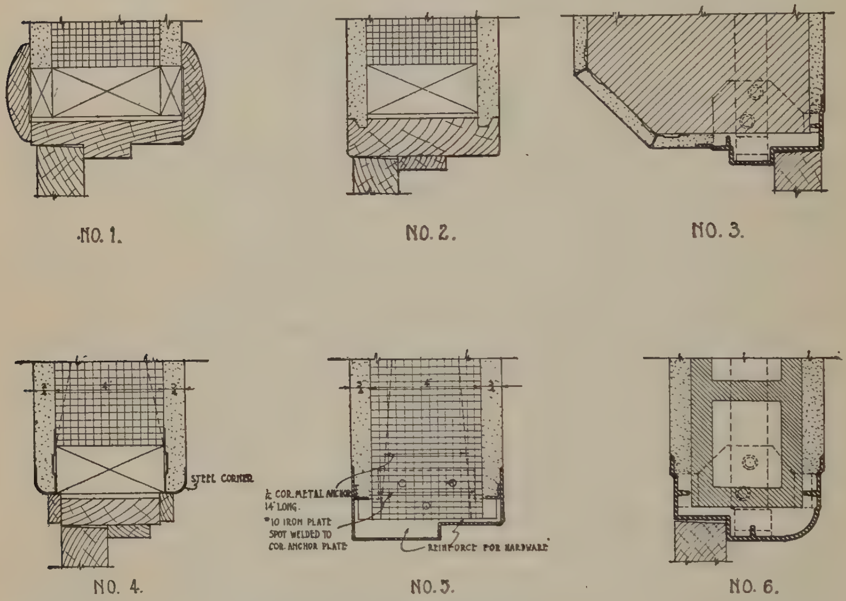


Fig. 228.—Door and partition window architraves. No. 1. An adaptation of ordinary wood casings to hospital use. No. 2. Flush wood frame which will probably curl and open cracks where the plaster joins it. No. 3. Combination of rolled steel flush frame and splayed angles. No. 4. Combination of wood and sheet steel. No. 5. Reinforced sheet steel frame and casing. No. 6. Rolled steel frame and casing with rounded angle and flush with plaster.

Special care should be used to build the brickwork tight against the frames, but as the water of the mortar swells untreated wood it is necessary to have the frames well painted before brickwork is laid against them. In buildings of monumental character window and door frames are sometimes set after the mason work is completed. In such cases it is necessary to build special iron anchors into the masonry, draw the frames tight to the brickwork to permit caulking the outside joint with oakum. It is well to remember that caulking is not effective unless the frames are held securely by iron anchor bars.

Weather Strips.—Metal weather strips are almost a necessity to prevent the ingress of dust and soot in smoky localities. There are many kinds on the market and only the best are economical over a number of years.

Window Casings.—Inasmuch as it is advisable to limit the amount of woodwork, windows are generally finished on the interior with steel corners and plastered jambs and heads. Marble or slate stools are preferable to wood, which constant wear soon disfigures (Fig. 225).

Door Casings.—The ordinary molded wood dwelling house door casings were modified somewhat as shown in Section 1 of Fig. 228 to and cleanliness and economy in house-keeping labor have been first given consideration. Then Section 2 was devised to eliminate projections, but that arrangement requires plastering after the frame has been set, but notwithstanding that the wood has been well painted it is very likely to curl slightly, produce cracks or joints between the wood frame and the plastering.

Rolled steel casings like Sections 3 and 6 of Fig. 8 are not affected by moisture, and are undoubtedly the best sections for the purpose.

Casings of sheet steel are made like Section 5 and are cheaper than No. 3 and No. 6 but do not have their appearance of solidity.

Section 4, a combination of drawn steel and wood, is economical and quite efficient.

Radiator Recesses.—Radiators can be placed advantageously and space saving, also most efficiently in terms of heating, by providing radiator recesses under windows (Fig. 229), allowing the stool to form a top, a single wire screen across the front and returning on the ends to the base of terrazzo or other impervious material in and around the back of recess and extending the border flooring into it.

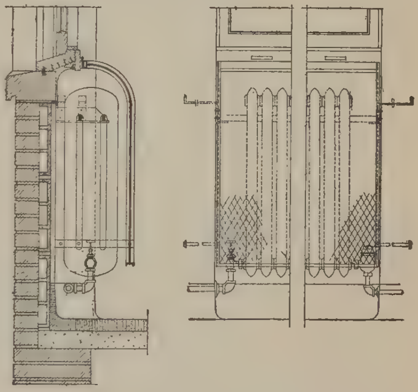


Fig. 229.—Radiator enclosure, suspended legless radiator in a recess under a window. Special guard of heavy woven wire in a light steel frame to prevent contact of children with radiator. Guard is hinged on underside of window sills to facilitate the cleaning or decorating of radiator or wall surfaces.

Sash Chains.—Chains for balancing windows require special pulleys, but are much more durable than cords. If the chains are of steel they must be heavily copper plated to prevent rusting

Introstiles.—French windows leading to porches and terraces must have special water bars, which are illustrated in the details of windows or introstiles, which seal the space between the floor and the bottom of the door, and which raise and close automatically with the operation of the door.

Insect Screens.—Re-wirable metal screens of the sliding type are more desirable than wood-framed screens, or metal frames which are not re-wirable. Insect screening of different kinds of metal are preferable in the following order:

Bronze wire, pearl wire, painted galvanized and painted black iron wire. The mesh must not be too large nor the wire too fine. These matters must receive careful consideration in comparing bids.

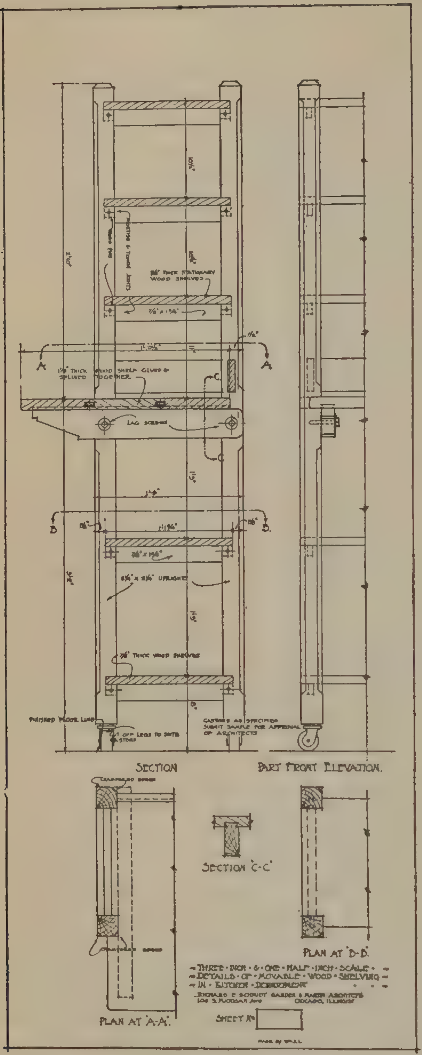

SECTION
PART FRONT ELEVATION.
SECTION 'C-C'
PLAN AT 'A-A'.
PLAN AT 'D-D'.
A
B
D
C
7/8" THICK WOOD SHELVES
FINISHED FLOOR LINE
CUT OFF LEGS TO SUIT STOPS
CASTERS AS SPECIFIED SUBMIT SAMPLE FOR APPROVAL OF ARCHITECTS
LAG SCREWS
THREE · INCH · & · ONE · HALF · INCH · SCALE ·
DETAILS · OF · MOVABLE · WOOD · SHELVING
IN · KITCHEN · DEPARTMENT
RICHARD E. SCHMIDT GARDEN & MARTIN ARCHITECTS
104 S. MICHIGAN AVE CHICAGO, ILLINOIS
SHEET No

FIG. 230.—Portable shelving. Unit sections of shelving on casters can be inspected and readily cleaned on all sides, arrangement variable and can be moved into other rooms or closets at will.

Doors and Cabinet Work.—Economy in operation, *i.e.*, janitor's service, requires the elimination of corners and projections wherever possible. It is for this reason that flush doors and flush trim, either wood, metal or a combination of these and plaster, is usually selected, and cabinets recessed without exposed tops. Flush doors should be built up of at least five ply; an inner core of strips of pine or other soft wood glued together, a veneering of hardwood, laid horizontally or cross banded and outer layers of hardwood, applied vertically. Cabinets and cases should be of wood or metal set on bases of the same material as the baseboard of the room in which they are located.

Sound Proof Doors.—Special sound proof doors are useful in some places. These are really two doors with a narrow space and felt between and a pantagraph arrangement of steel bars which braces strips of felt against both sides and top of the frame and against the floor when the handle is moved. This is a patented device which has been used in many hospitals and other buildings where sound proofing is a requisite.

Dutch and Screen Doors.—Doors cut into two parts horizontal about in the middle of their height, commonly known as Dutch doors, are useful for observation and ventilation, also in preventing children from leaving a room. Interior screen doors consisting of a light frame-work covered with removable and washable muslin curtains are useful for private rooms (Fig. 232).

Shelving.—Metal or slate shelving is desirable on account of its cleanliness, but it is so expensive and difficult to move and reset to satisfy changing conditions that wood is usually employed, and to make it convenient to move it about, it is often built in movable units, on castors as illustrated in Fig. 230. Perforated metal channels of the kind devised for show windows is an excellent support for adjustable shelves in linen closets and other store rooms. Light steel sections, similar to the kind shown in Fig. 231, are bolted to the partitions and are flush with the plastering after that is completed. The shelves can be removed or the spacing changed by lifting the brackets out of the keyhole-shaped perforations in the wall channels.

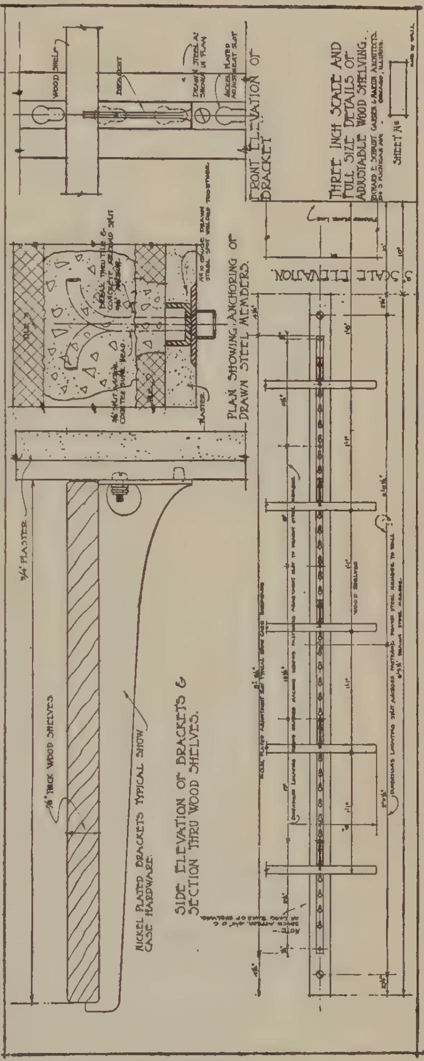

FRONT ELEVATION OF BRACKET
THREE INCH SCALE AND FULL SIZE DETAILS OF ADJUSTABLE WOOD SHELVING.
SHEET No
PLAN SHOWING ANCHORING OF DRAWN STEEL MEMBERS.
SCALE ELEVATION
¾" PLASTER
⅞" THICK WOOD SHELVES
NICKEL PLATED BRACKETS TYPICAL SHOW CASE HARDWARE.
SIDE ELEVATION OF BRACKETS & SECTION THRU WOOD SHELVES.

FIG. 231.—Adjustable shelving. A commercial show window device. Spacing of shelves can be readily altered or removed by raising them to the top of the "keyholes" punched into the vertical channels which are built into the walls.

Wood Finishing.—White enameled woodwork is most attractive but suffers greatly by the constant cleaning required to maintain it immaculately white, consequently, hard woods finished to show their grain will be most generally used.

Soft woods enameled suffer too much from the impact of furniture and other things, making it necessary to use hard wood. Enameled woodwork consequently costs as much as some of the cheaper hard woods, such as birch; possibly it costs a little less than oak. Good durable enameling costs more than filling, shellacing and varnishing for natural finish or stain finished hard wood.

Door Silencers.—A rubber silencer is an improvement on the cloth husher which nurses tie from knob to knob over the latch, but either of them makes the latch functionless and proves convincingly that ordinary locks and knobs do not fulfill the desired function.

Door Hardware.—A good door spring and check for a door 42 in. wide, the least width suitable for moving a bed 3 ft. wide from one room to another, costs about $7.50 and makes a large bill if applied to every door.

Figure 233 illustrates a patented device wich apparently makes a check unnecessary, accomplishes the same result and improves the appearance, if the soft rubber bumper, which is a part of the arrangement, is replaced when it is worn out. The spring bolt and special strike plate holds the door closed. This arrangement requires a knob or preferably a hook on both sides of the door. Friction hinges will hold the door open in any position with sufficient strength to resist drafts.

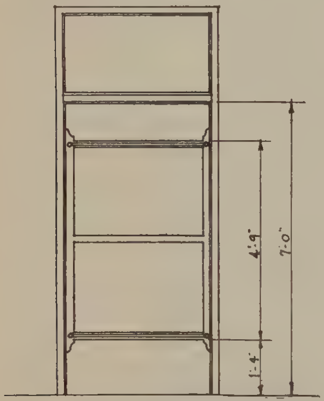


Fig. 232.—Interchangeable half or screen doors for ward doors: A wood frame with curtain rods, covered with washable natural linen.

Casters.—The damage done by ordinary furniture casters to linoleum, mastic, rubber and other kinds of elastic floors can be prevented by using metal sliding shoes in place of casters, or by placing these in glass shoes. Both of these slide so smoothly and easily that the heaviest pieces of furniture can be moved in any direction.

Transoms.—Wood paneled door transoms are not as objectionable as glazed transoms but neither stop the passage of light when the transoms are open. This kind of ventilation can be obtained without this objection by using one of several devices manufactured for the purpose, such as Ventilouvres and Ventadoors, which are metal frames for placing into door panels or into openings in the wall above the door; they are fitted with Z- or U-shaped pieces of metal, which prevent the passage of light and can be rigidly set for various degrees of ventilation or fully closed (Fig. 234).

Bed Screens.—Folding or straight screens to place around or between beds can be made of tubing similar to metal bed tubing and the panels covered with painted woven wire, in place of cloth covered wooden frames. They call the attendant's attention to doing those things which are necessary for proper isolation and are not only slightly more transparent than cloth screens but obviously require less maintenance or replacement.

Beds can also be obtained with high posts and swinging screens on one side and the foot to divide a ward into cubicles.

Double Glazing.—Obviously vitiated cold air is fully as harmful as warm air, and it is also obvious that there would be a saving in fuel cost if heat losses through the glass of windows were reduced, inasmuch as this does not supply pure air or improve its condition. The heat loss should not be confounded with the loss due to poorly fitting sash, which provides a supply of fresh air where no other provision for obtaining it has been made. The heat loss through ordinary glass is almost 10 times that through a good wall and a great saving in fuel could be effected if it were prevented. The waste can be practically reduced and condensation of moisture and consequent frosting avoided by the use of storm sash. These, however, are usually unsightly, expensive in maintenance and make proper window ventilation and cleaning difficult.

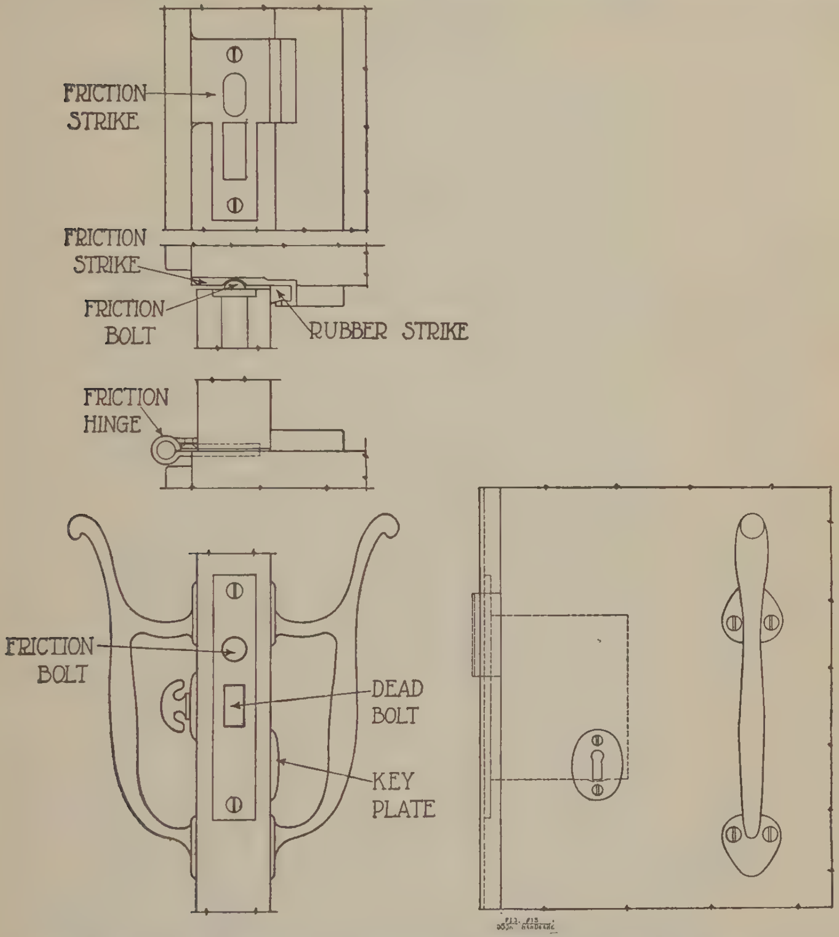
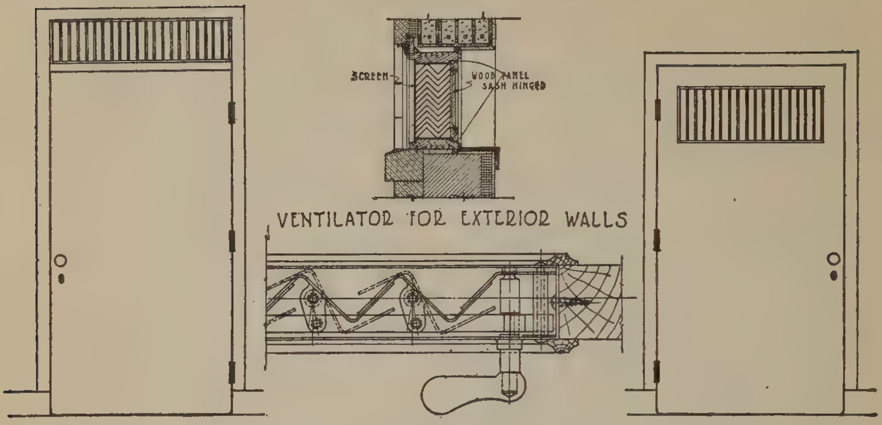


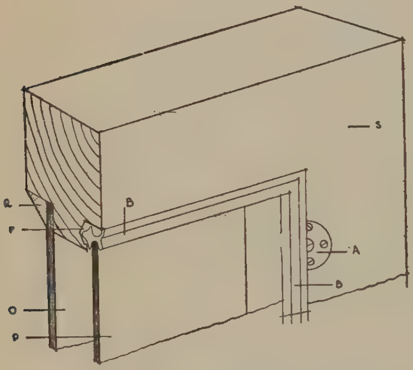
Fig. 233.—Door hardware. Doors can be opened or closed while both hands are engaged in carrying a tray or other object. Friction hinges hold door in any position. Friction bolts close door inaudibly against rubber strikes, locked from inside by latch and opened by a simple key. Applying hooks downwards may be preferable to having them turned upwards.

About 20 lb. of coal per year per square foot of window can be saved by providing two thicknesses of double strength glass with a

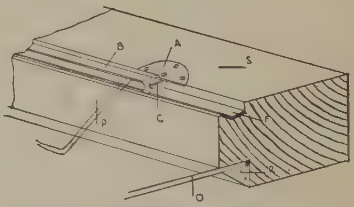


VENTILATOR IN TRANSOM VENTILOUVRE VENTILATOR IN DOOR

FIG. 234.—Lightproof metal ventilators for wards, *x*-ray, eye department and photographic rooms.



SECTIONAL VIEW OF SULL SASH
S. SASH. O. OUTER PANE. P. INNER PANE
B. GLAZING BAR. A. FASTENERS
F FELT. R PUTTY.
PATENTED OCTOBER 22, 1918.



CUTAWAY SECTIONAL VIEW THROUGH
POINT OF FASTENER C SWIVEL ENGAGING
BAR PATENTED OCTOBER 22, 1918.

FIG. 235.—Sectional view of a double glazed sash, the inner glazing secured by the sull metal frame and turn buckles.

sealed air space between them, instead of the ordinary single thickness of double-strength window glass, where the average outside temperature during the heating season is approximately 35°F., which is the average heating season temperature of Chicago. At the present cost of coal and labor, there would be a saving in excess of an interest charge on the cost of the extra glazing and an annual replacement charge. The sizes of radiators, valves and piping can also be reduced, and the saving effected thereby would pay the cost of cleaning the additional glass.

The benefits of storm sash without their objections can be obtained by glazing the sash with two lights of glass, but notwithstanding that every care is used in setting the glass a considerable percentage does not remain air-tight, dust passes into the enclosed air space and cannot be removed from the inner surfaces of the glass without removing putty and resetting after washing, the cost of which with painting and other incidental work aggregates a considerable expense and much inconvenience. A recent invention (Figs. 235, 236) consists of specially drawn zinc strips forming a frame for the inside sheet of glass, in combination with a felt lined groove in the sash and a flush metal arrangement which holds and presses the metal frame into the felt lined groove making it possible to remove, wash and reset the inner sheet of glass quickly and easily. Manifestly this cannot be applied to old sash.

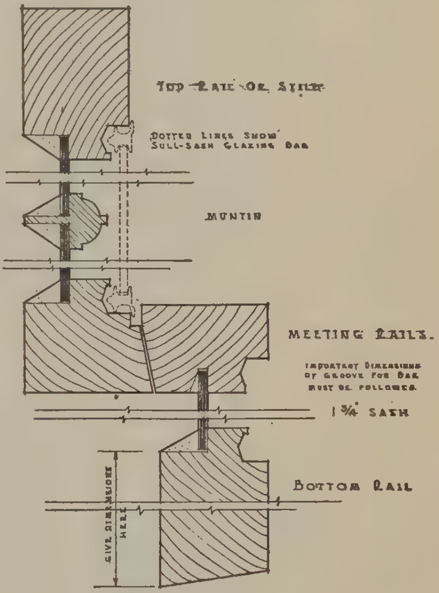

TOP RAIL OR STILE
DOTTED LINES SHOW SULL-SASH GLAZING BAR
MUNTIN
MEETING RAILS.
IMPORTANT DIMENSIONS OF GROOVE FOR BAR MUST BE FOLLOWED
1¾" SASH
BOTTOM RAIL
GIVE DIMENSIONS HERE

Fig. 236.—Details for sull sash.

Food Conveyors.—Very efficient food conveyors or carts based on the principle of the fireless cooker, i.e., thoroughly insulated, have recently been developed. Food fully as palatable and hot as it would be if served directly from the ranges can be served from them at a great distance from the kitchen and a long time after it has been cooked. Figures 237, 238 illustrate two of the best types, both arranged for conveying food in bulk with shelves for clean or soiled dishes.

A new type of conveyor carries food on plates direct from kitchen to patients' bedside. The capacity is 15 to 24 plates in wire trays. The plates are placed in wire racks and the racks in insulated conveyors. There is also a compartment for wet vegetables in addition to the regular plate dinner; these are put on individual dishes and also placed in racks. This type differs from the one in which food is carried in

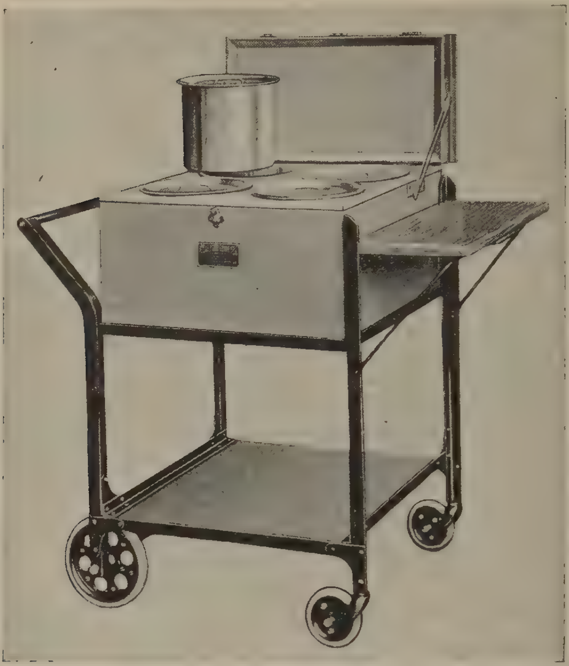


FIG. 237.—Bulk food conveyor.

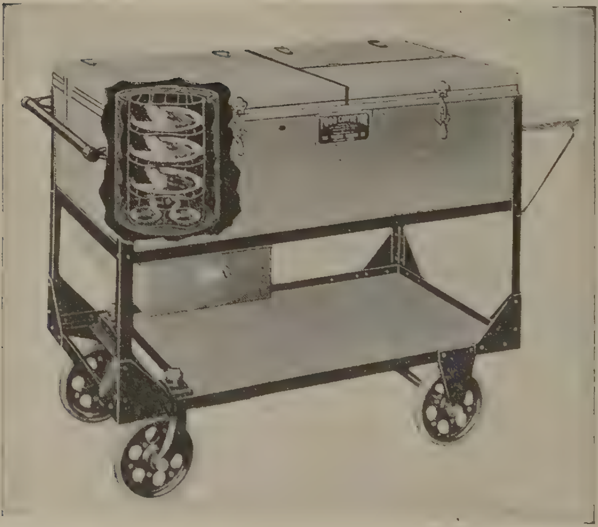


FIG. 238.—Bulk food conveyor.

bulk by having deeper pockets and substituting wire racks for the aluminum utensils. Hot food conveyors should be preheated by placing soapstone radiators inside of the compartments a few minutes before inserting the food, and cold food conveyors should be precooled in extremely warm weather. While it is possible to carry cold and hot food in the same conveyor, obviously not in the same compartment, it would be better to have separate conveyors for hot and cold food. Figure 239 illustrates the plate conveyor; the drawer is for silverware. The plate conveyor seems most desirable for private room service in a hospital for adults, but not a necessity in a children's hospital.

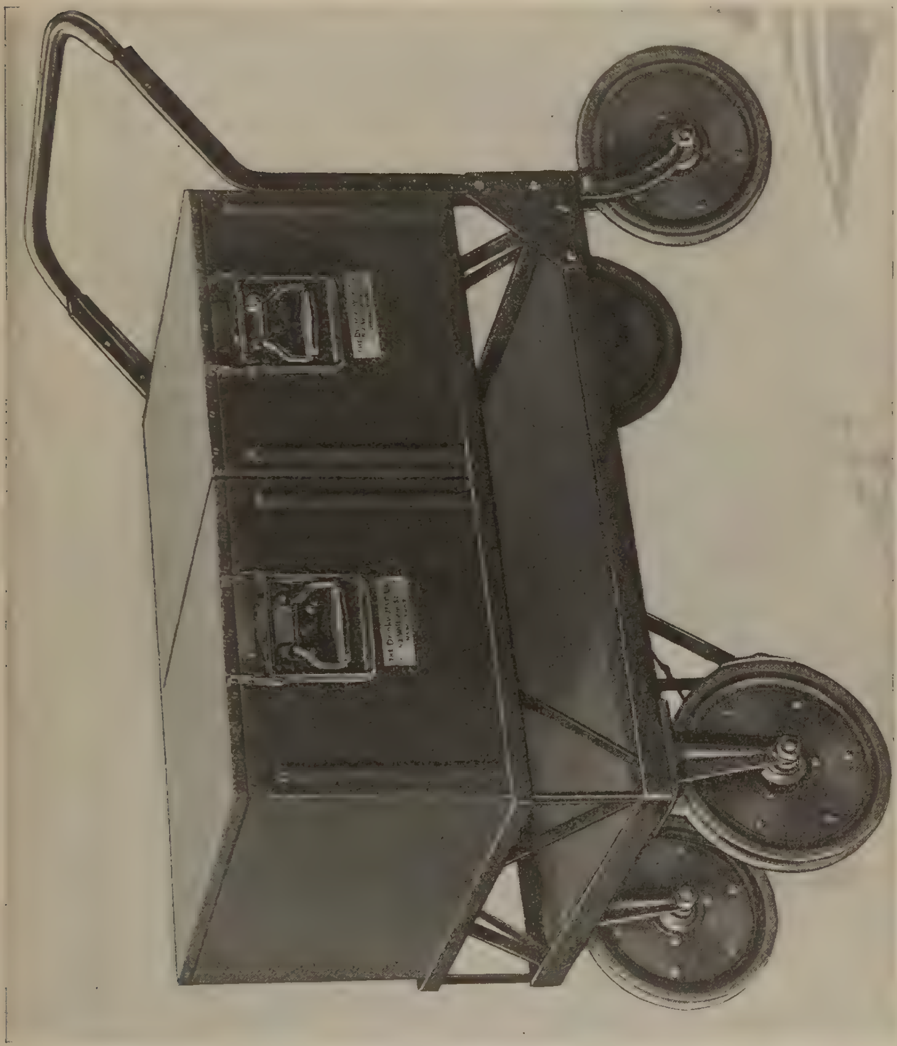


Fig. 239.—Drinkwater food cart with removable boxes of a set of containers. The boxes are interchangeable and the cart will not be idle while the boxes are on the floors.

Serving food direct from a bulk food conveyor in wards or children's day rooms is manifestly labor saving and economical in food.

Mechanical Equipment.—The problems of sterilization, heating, ventilating, cold and hot water consumption, the variety of uses of refrigeration, electricity, etc., differ totally in hospitals from other classes of buildings; the data necessary to properly design these services is available only to those who have had experience in the building of innumerable institutions and observing their sufficiency or failure to meet the requirements

Boiler Room and Power Plant Equipment.—It is essential that steam should be furnished for heating, sterilizing and cooking purposes, also for proper operation of the laundry, and it may be used to advantage for heating hot water for domestic purposes. The pressure of steam required for sterilizing and laundry work is from 60 to 90 lb. The pressure best adapted to cooking and general kitchen use is in the neighborhood of 25 lb. The heating system requires low pressure steam as a general thing, a few ounces for a modulating system, and seldom exceeding 2 lb. in the other types of systems. The heating of hot water for domestic purposes may be accomplished by either low or high pressure steam. The hot-water heater can be designed to meet the requirements best adapted to the plant. In the case where cast-iron boilers are used for heating systems, they are only in use in the neighborhood of six months of the year, and in addition a small high pressure boiler would have to be kept in operation throughout the year to supply high pressure steam where needed. This means two fires burning for six months of the year, which entails considerable loss in fuel consumption. A large cast-iron boiler has large open horizontal passes, and soot collects on these flat surfaces very rapidly and affects the efficiency considerably. It is also to be noted that the efficiency of the cast-iron boiler is a matter that even the makers appear to know very little about.

The use of low-pressure steel, brick-set, firebox boilers to take care of the heating system is no doubt a somewhat more efficient boiler than the cast-iron type. This type of boiler has a steel drop box water leg section surrounding the firebox; the gases from the fire pass through the tubes and over or under a portion of the exterior surfaces of the boiler. When bituminous coal is burned in these boilers, the tubes collect soot quite rapidly and the space between the brickwork and the outer shell of the boiler becomes clogged with soot. If the fireman is careless and does not remove the soot from the tubes and the smoke passages of the boiler frequently, the boilers become clogged to such an extent that their efficiency is low and the possible saving to be made over that of the cast-iron boiler is lost.

In the case of the small vertical high-pressure boiler we also have a boiler that is very inefficient, and the labor and attention the fireman has to give these boilers in order to get their rated output out of them is excessive. The percentage of fuel in the ashes is surprisingly high. Experience shows that it is desirable when using small high-pressure boilers to have the rating of these boilers 300 per cent. or more above the actual requirements.

The use of cast-iron boilers means that cheap grades of bituminous coal cannot be used successfully, without creating a lot of smoke and clogging of the boiler with soot. The fuel best adapted to use in these boilers is the semi-bituminous coal from West Virginia; the kind called Pocahontas or pea anthracite coal may be used. In the case of the small vertical high-pressure boilers, it is impossible to burn even semi-bituminous coal smokelessly and in order to have smokeless combustion in the small high-pressure boiler it is necessary to provide a brick setting in which special provisions can be made to eliminate the smoke.

Taking into consideration economy and smokeless operation, it is considered advisable in the majority of cases to design plants with large brick-set boilers in which the cheap grades of fuel can be burned efficiently.

Selection of Boilers.—The size of the hospital is a determining factor in selecting the size of the boiler. The small institutions in which combined sterilizing, cooking and laundry, and domestic hot-water supply requires less than 150 hp. and the heating load does not exceed 150 hp., it would be advisable in most cases to use brick set horizontal return tubular boilers. Return tubular boilers are seldom built for a larger capacity then 150 hp.; they can be set in individual settings or in a battery setting, and a boiler room containing four of these boilers in which three are required to carry the steam load, permitting the shutting down of one for cleaning and repairs, would be a plant in which the first cost is low, and in which a cheap grade of fuel can be burned efficiently.

Water tube boilers are generally considered and adopted when the individual use of a boiler plant exceeds a rating of 150 hp. Such boilers can be built of capacities up to 2000 hp. However, it is doubtful if it would be advisable to use larger than 500 hp. for a hospital.

Water tube boilers are constructed of tubes, tanks, baffles and brickwork, and the life of such a boiler is generally considered much longer than that of a tubular boiler. Portions exposed to the fire are the tubes and the baffles, and in the event of the failure of either one, they can be replaced quite easily. For this reason and because the tanks rarely develop defects, a water tube boiler generally requires only minor repairs.

Stokers.—Coal has advanced in price the last few years, and it may never return to its former price. The high price of fuel makes it worth while to consider the question of stokers. In the case of water tube boilers, mechanical stokers show a saving over hand firing. There is a great difference in coal from different sections or even from different mines in the same district, consequently a special study of the fuel to be used should be made before selecting the type of stoker. The chain grate type of mechanical stoker will handle a wider range of fuel than the underfed type of stoker. The high price of coal has brought out special air control devices, which will enable the fireman to cut down the excess air going through the burning fuel.

Grates.—Hand fired boilers should have rocking grates. In the case of hand fired boilers or one having automatic mechanical stokers, the efficiency of the furnace depends in a large measure on the quality of the fireman. In order to get the best results out of coal burned the fireman must be on his guard at all times; the engineer should keep a check on the coal burned, for the average fireman has no incentive to save coal, all he thinks of is to keep up steam and make his own work easy, for the owner is buying the coal.

Meters.—Up-to-date boiler plants are equipped with a recording steam flow meter, and a means of weighing the coal. When the engineer or superintendent has a daily record of the water evaporated and the coal burned he can easily check up on the quality of the fireman or detect any other cause of loss that may develop in the plant.

Soot Blowers.—Soot blowers to clean the tubes of a return tubular boiler or the various passes of water tube boilers should be installed so that the fireman can keep the boilers clean and working efficiently. This is especially true where bituminous coal is used.

Boiler Setting, Breeching and Stack.—Each type of boiler requires a special study of the brick setting in order to give the best results. The aim should be to have a hot fire in the furnace to consume the smoke and to so arrange and proportion the path of the hot gases that they will travel through the boiler in contact with the surfaces and pass into the breeching at a low temperature. The size and height of the stack, the shape and size of the breeching, should be such that they will insure a sufficient draft to overcome the friction in the boiler and fuel bed, with enough reserve to take care of sudden loads and an excessive overload if necessary.

Engine Room Equipment.—In designing a hospital power plant, one of the problems to be settled is the advisability of installing engines and generators or to buy current for light and power from the Public Service Company.

A hospital requires heat seven months in the year and as the heating load is greater than the lighting and power load, the exhaust steam from the engines is not sufficient to take care of the heating. The percentage of heat taken out of the steam in passing through the engine is small, so that during the heating season the cost of generating electric current is very low. During the summer months the days are longer and the percentage of electricity used for lighting is considerably smaller. By using exhaust steam for heating water for domestic purposes it is surprising how little exhaust steam is wasted even in the summer time.

There are other things to be considered besides the cost of coal, labor, upkeep and depreciation. The engine room help are employed to a great extent in maintenance work in the hospital proper. It is surprising the amount of repair work the engineer can do and in a great majority of cases he puts in more than 50 per cent. of his time making repairs or doing maintenance work on hospital equipment.

After making a careful study of the individual conditions, taking into consideration all of the costs of operating, it will be found advisable to install a complete power plant, including engines and generators, in a hospital having 100 beds or more. The choice between direct current or an alternating current plant will have to be made before the final stages of the plans are reached. Direct current machines are better adapted to a small plant where elevators and other motors are used, for the reason that the regulation of the small direct current generator is by far better than the alternating current machine; again, direct current motors make less noise. In case alternating current generators are used a good grade of voltage regulator should be added to the plant to aid in the regulation.

The smaller engine room equipment, such as pumps, feed water heater, etc., should be of a good grade specially selected for the work they have to do. Simple reliable automatic governor devices should be installed; all pumps and engines should be equipped with force feed oiling devices keeping in mind that the work in the engine room should take up only a small portion of engineer's time. The engine room should be large enough so that a work bench can be installed where the engine room force can make engine room repairs and also do the repair work on the hospital equipment.

All steam and return lines between the power house and the hospital should be installed in the shortest direct line to apparatus they supply. The shorter the steam lines the smaller the loss. Starting from the boilers under boiler pressure the lines to the boiler header and the header itself should be as short as conditions and a proper allowance for expansion will permit. Separately valved lines should be taken from the main steam header to the engines and larger steam using units so that when the machinery is not in use the steam line can be shut off at the header.

The sterilizers in a hospital require 60 to 90 lb. steam; a branch line should be taken off this line through a reducing pressure valve to supply the kitchen equipment with 23 lb. steam. In the majority of cases the following steam lines should supply the needs of a hospital: One 60 to 90 high-pressure steam line, one high-pressure trap return line, one exhaust or low-pressure steam supply to the heating system and one heating system return. Four inch and larger valves and fittings should be flanged and in restricted spaces such as pipe trenches or small tunnels the pipe lines should be flanged. In order to keep down the cost of maintenance all gaskets of both high- and low-pressure lines should be of the best grade.

All fittings on lines facing boiler pressure above 125 lb. should be extra heavy fittings. Fittings for use on the remainder of the system should be standard weight cast-iron fittings. As a general thing, standard weight pipe can be used when the boiler pressure does not exceed 125 lb. working pressure. With boiler pressure above 125 lb. it would be advisable to use "extra heavy" pipe.

The life of the pipe under any installation depends substantially upon the local water conditions, and it is quite important to take this into consideration when the plans are being designed. Standard steel pipe of the market under certain conditions deteriorates very rapidly. Standard wrought-iron pipe which is made of a purer grade of iron has a considerably longer life and should be used where conditions warrant it. In the modern hospital, conditions of sanitation and appearance demand that a great many of the pipes shall be concealed in the partitions and behind furring. Pipes so concealed should preferably be wrought iron for if of steel the cost of replacement would be large.

Heating.—The comfort of patients in a hospital depends for a larger portion of the year upon proper and effective heating of the rooms. This must be done in a way that will require a minimum of maintenance, be noiseless in its operation, and should be easy to control. Special consideration should be given to the details and locations of the heating units to insure cleanliness.

The general heating of hospitals is accomplished by the use of direct radiation distributed adjacent to the exterior walls and proportioned according to the amount of exposure. Hot water heating if by gravity or forced circulation has certain advantages of control in its favor, due to the fact that the temperature of water can be varied in accordance with the outside temperature changes. This is especially true with forced water circulating systems, where a pump of some kind is used to keep the water in circulation. The disadvantage of using hot-water heating systems is, that the radiators are a great deal larger and the cost of such an installation is greater than steam.

Steam heat is more extensively used in hospital work and there are several distinct systems and among the ones in general use are the simple gravity system, having single pipe risers. This system is the least expensive and can be used to advantage in small hospitals where pipe runs are short. One of the disadvantages of this system is that the air from the radiators has to be expelled through individual vent valves on each radiator and the odor of steam may be noticeable in the rooms at times; further, these vent valves if not regulated properly are apt to make considerable noise and in a great many instances expel water at times. It is hard to keep the best grade of vent valves operating for the reason that the occupants of the room tamper with them a great deal.

The vacuum system of steam heating is one that can be applied to any kind of condition and is especially adapted to an institution that covers considerable ground or requires long horizontal runs of piping. This system consists of low-pressure steam piping and risers extending up through the building supplying steam to one end of all the radiators and a return system of piping starting from the opposite end of the radiator paralleling the steam lines and terminating in a vacuum pump located at some low point in or adjacent to the power house. In the case of a vacuum system special thermostatic temperature valves are placed on the return opening of each radiator. These traps allow all the water of condensation and air to pass into the return piping, but are so adjusted that they will prevent steam vapors from flowing into the returns. In the vacuum system the vacuum pump maintains a vacuum of any required amount upon the return system and discharges the water of condensation and air into a drip tank or other special device for eliminating the air, the water of condensation being returned to the feed water heater. This system eliminates the necessity of vent valves and with the vacuum pump working on the return lines is the most flexible steam heating system available.

The lines can be run with less pitch for drainage, and where run through the basement where it is important to maintan head room, the low points in the main can be drained through vacuum specialties back into the return lines and the return lines when necessary can be placed without downward inclination and, moreover, they can be revised slightly, if necessary, by the use of special lift fittings.

Modulating systems of steam heating can be installed where the horizontal area to be covered is not too great. This system is a two-pipe system, having steam and return piping corresponding with a vacuum system and thermostatic return valves on each radiator similar to the vacuum system. The modulated system depends for the expulsion of air upon filling the system with steam, the water of condensation and air being carried down through the return pipes to the boiler room were the air is expelled by specially designed air eliminating traps. This system is generally operated on only a few ounces of steam pressure. One of the excellent features of this system is the control valve on the steam inlet to each radiator. These valves are graduated with a pointer which indicates on a dial under the handle the degree of opening in the valve. These graduations are generally marked ¼, ½, ¾ and full openings. The principle of their operation is that the opening in the valve when set on ¼, for instance, will only allow enough system to pass the valve to heat one-fourth of the radiator, and when open full, the steam will fill the entire radiator. Such a system if perfectly installed has advantages of control superior to any other system. It requires larger pipe sizes and needs more careful attention in laying out an installation and because of the low pressure used, the main must have a greater inclination and the returns must incline to the air eliminating traps; this makes the system less flexible and more expensive than the vacuum system. It is easier to clean radiators having plain smooth surfaces than it is those which have an ornamental design, and for this reason plain radiators should be given preference. There are on the market standard radiators having high legs and large spacing between the sections, these radiators when set 3 in. from the wall are fairly easy to keep clean and it is possible to paint the walls without removing the radiation. Legless radiators (Fig. 9), which are supported on specially designed brackets behind the radiators, make the best possible arrangement from a sanitary point of view. The steam and return pipes to and from the radiator should extend directly to the wall, leaving the floor and base easy to clean. In order to keep children from coming in contact with the hot surfaces a specially designed hinged heavy wire guard should cover the entire radiator. These guards should be so arranged that they will allow the radiators to be cleaned.

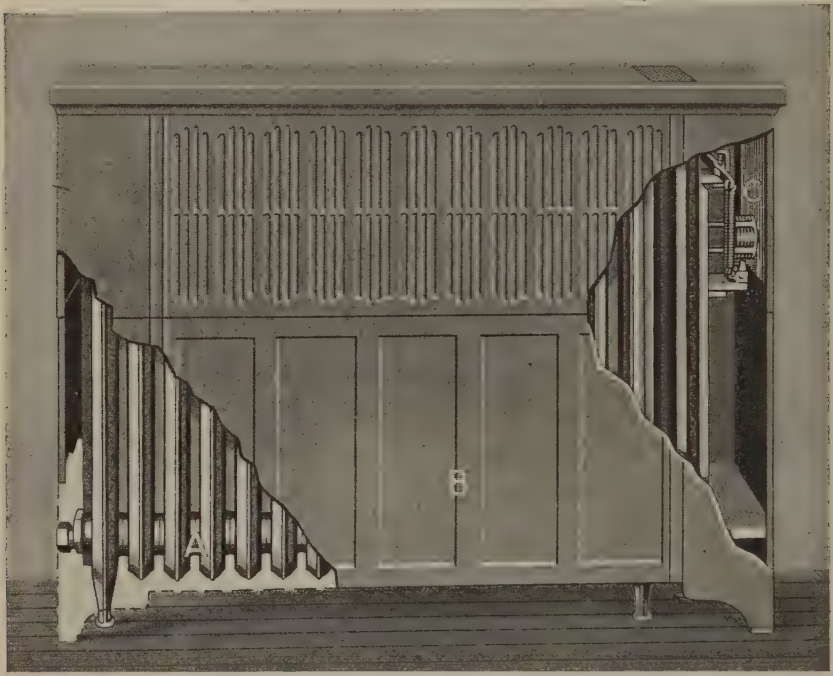


Fig. 240.—Thermostatically controlled radiator enclosure.

In some places in the hospital, it may be appropriate to use a more ornamental radiator enclosure, in the order of the one shown in the cut. This enclosure is made of furniture steel, open at the bottom and perforated in the front. The coolest air being at the floor, it enters at the bottom of the enclosure, as its temperature rises it flows upwards and out into the room away from the walls and draperies through the openings in the front, saving these to some extent from dust.

The temperature is controlled by a thermostat placed in a separate compartment of the cabinet, entirely insulated from the radiator, and so arranged that it responds only to the temperature of the air in the room. If the temperature falls, the Sylphon Thermostat opens a series of shutters inside the cabinet, permitting more heated air to issue into the room—as the temperature rises, it automatically closes these shutters, maintaining an even temperature in the room.

The Sylphon Thermostat may be set for any temperature desired between 60 and 80 degrees. Each is a separate unit, permitting the holding of a different temperature, as may be desired in every room which contains one of these units.

An interesting feature of this device is that it is actuated by expansion and contraction due to fluctuating temperature, instead of expensive electrical connections or mechanical appliances.

The cut shows the thermostatic control at "C" which is located behind a small louvre in the end of the radiator enclosure. The air entering at this point passes over the thermostat and cut of the small register shown in the top.

Temperature Control.—In the operating department and nursery, where a uniform temperature is desired, it may be advisable to install automatic temperature control valves on the radiators; these valves are operated by thermostats located in the rooms.

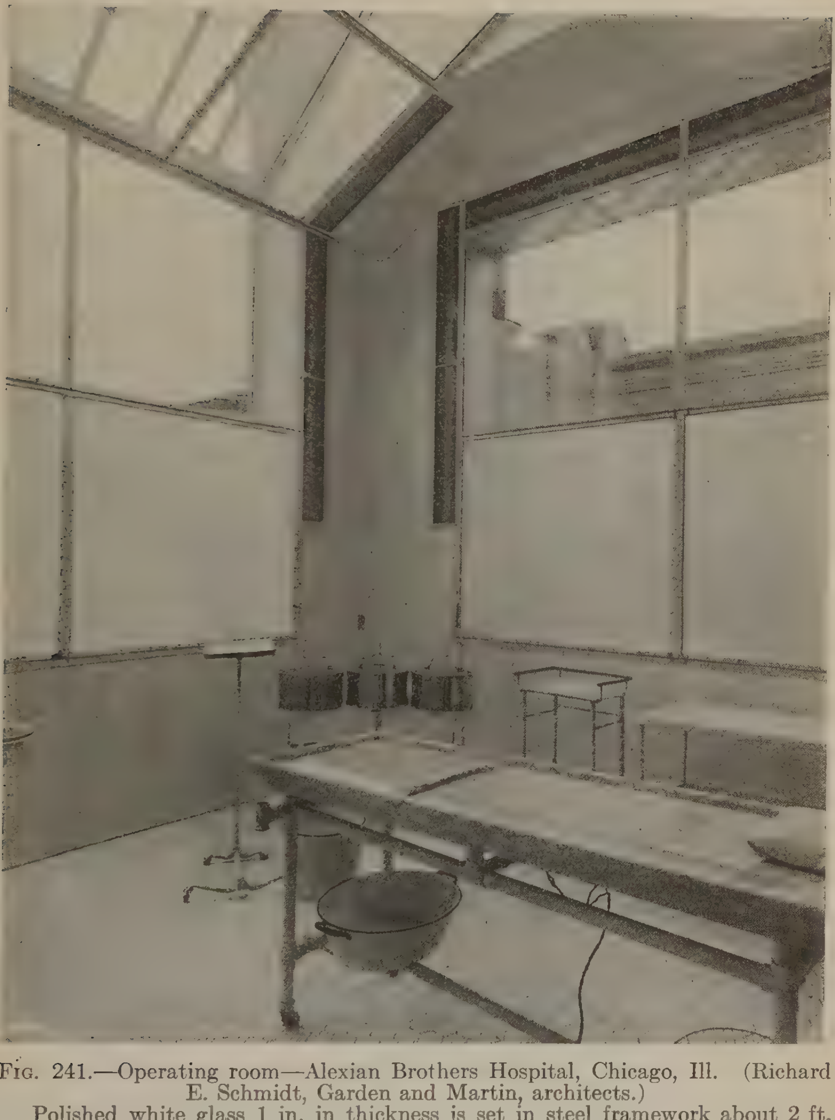


FIG. 241.—Operating room—Alexian Brothers Hospital, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

Polished white glass 1 in. in thickness is set in steel framework about 2 ft. from the brick enclosing walls. Sides and top of window recesses are also lined with white glass, and the bottom or sill with perforated metal.

There are steam heating coils in the space between the white glass and brick walls and no other means of heating are provided. The air is exhausted by fans. The room is illuminated at night by flush trough boxes; all sash are double.

The latter types are preferable provided they are not too hard to operate.

Radiators.—Proper distribution of the radiators should be made to heat the rooms comfortably and in general it is best to locate them under the windows (Fig. 229). The amount of radiation should be figured carefully, taking into consideration the glass area of windows and other exposures so as to get uniform heat throughout the hospital.

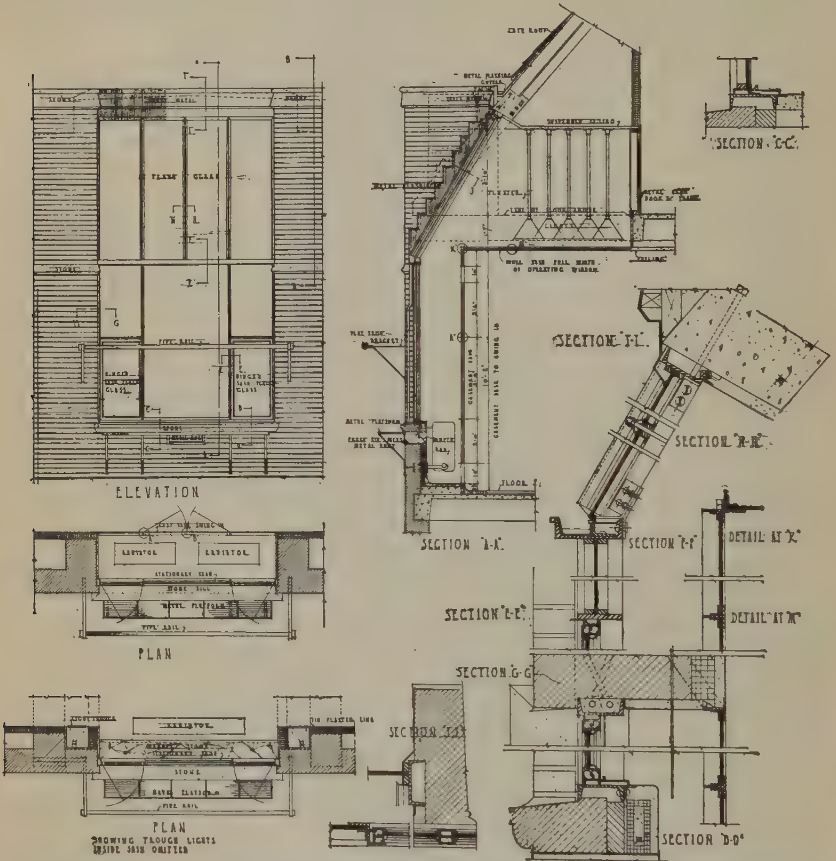


Fig. 242.—Details of operating room windows. Section A-A illustrates a double glazed operating room window with illuminating units over a ceiling light, and heating units between the inner and outer sash, and gallery and safety railing for cleaning the outer windows and skylights.

In general throughout the hospital, the manual control steam valves should be a good grade of valve with heavy wood handles. These valves can be either the standard packed valves or the packless type. Large rooms can be more uniformly heated by using several small radiators, rather than one large one (Fig. 240).

Concealed Radiation.—Heating of operating rooms by means of heating coils, concealed in the surrounding walls, is an ideal arrangement, removing as it does the radiators, which require so much labor for cleaning. Some of the sections of Fig. 242 illustrate details construction and Fig. 241, a photograph of an operating room.

The principal rooms of the Army Hospital at Wiesbaden, Germany, are heated by coils in a space 3 ft. high under the floors, which are constructed of light steel and concrete surfaced with tile. These wards are comfortably heated when the outside temperature is 40°F. without raising the temperatures of the floors to an uncomfortable degree. When the outside temperature falls below 40 degrees, the heating is augmented by auxiliary radiators in the rooms. Air conditions are said to be very pleasant. An arrangement of this kind seems very desirable for children's play or play rooms and operating rooms, and it could very easily be installed in one-story hospitals.

Insulation.—Pipe covering of a good grade should be used, 85 per cent. magnesia covering for high-pressure steam, wool felt or air cell for low-pressure steam, hot and cold water lines. Covering is used to prevent loss of heat in the hot lines and sweating and dripping from the cold lines. In the case of steam lines concealed in the partitions they should be carefully covered or they will mar the decorations. The proper application of the covering is just as important as the selection of the covering. Many a job of covering is ineffective on account of workmanship, and such workmanship is generally hidden by the canvas covering and only a close inspection of the work will reveal the defects.

Ventilation.—Ventilation in a hospital resolves itself into three phases, namely, ventilation of the operating department, ventilation of service departments and ventilation of wards.

Ventilating the operating department is a matter requiring great care and exactness. Obviously, it is undesirable to supply air to operating rooms through long runs of inaccessible and dirt collecting ducts. Separate systems are recommended preferably for individual operating rooms, each with its own air washing unit. An alternate, though less desirable, scheme is to supply air to the entire department from one fan and washer, and filter the air as it enters each room through absorbent cotton laid on removable frames.

Drafts and infiltration of dusty and otherwise bad air from adjoining rooms and corridors must be avoided. As a general practice, where the operating department consists of several major operating rooms with adjacent anesthetizing and surgeons' scrub rooms, it is best to admit fresh washed air to the operating rooms, keeping them under a slight pressure and exhausting air, either with a fan or by means of natural vents through the adjacent anesthetizing or scrub rooms.

Ventilation of service departments, which includes laundries, kitchens, laboratories, toilets, morgues, serving rooms, diet kitchens, etc., is generally a question of exhausting air. Ducts connected to hoods over kitchen ranges and other cooking equipment are subject to accumulations of grease, and should be properly insulated to protect the building from damage by fire. Fans on kitchen exhaust systems should be provided with automatic dampers, which, in the event of fire in the duct, will automatically cut the fan out of the system.

Ward and sick room ventilation is best obtained by natural means in conjunction with special window ventilators, or depending on the open window. Experience has shown that this seems to be the most satisfactory to the occupants of the rooms. Fresh washed and heated air can be taken into the rooms and exhaust taken out by the exhaust system. This makes theoretically a perfect system but to educate the patients to feel comfortable with such a system and to satisfy them that the windows do not need to be open for their comfort or well being is very hard to do. It can be done, but in the absence of a perfect ventilating apparatus, they cannot be satisfied without the open window, which makes the bringing of fresh air into the rooms by means of a fresh air system a useless expense, unless it is of the very best type. In special places, where desired, direct-indirect radiators can be used. This method necessitates the introduction of outside air through a screened opening in the outer wall into the radiator close to the floor and some means of exhausting near the ceiling.

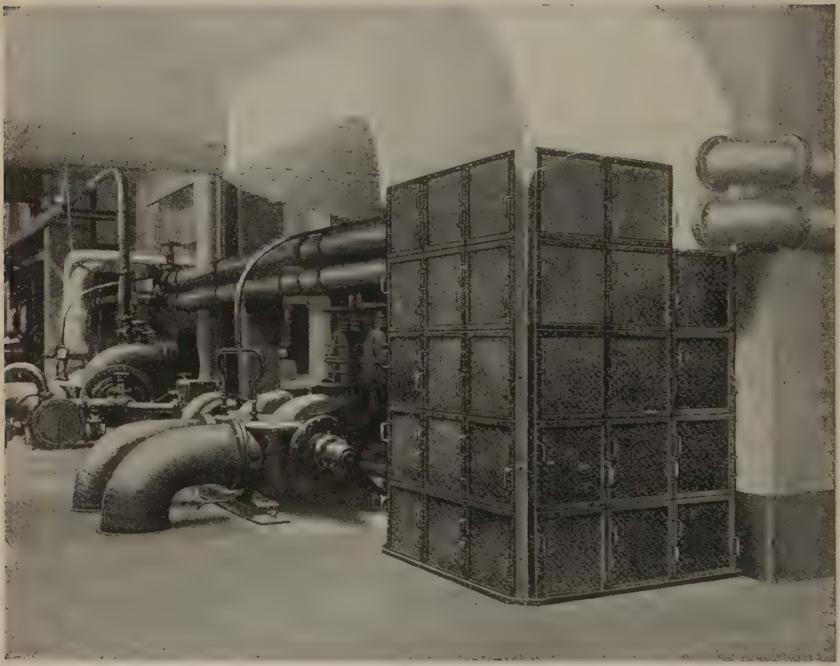


FIG. 243.—Midwest air filter. Dusty air taken from street level is drawn through filters and forced into the hospital.

These remarks regarding ventilation may not apply as much to children as they do to adults, but they are pertinent for hospitals for either age.

Air Washing.—The installation of a device to supply fresh air is a loss if it is not equipped with an efficient air washer. A tunnel or chamber containing a long water sprayed cheese cloth bag to obtain sufficient area has been found impractical. Its efficiency is too uncertain and it requires frequent renewal. A modern spray washer is efficient but cannot be recommended unless the hospital is large enough to employ a trained and experienced engineer to attend to the cleaning of the sprays and the electric motors and pump.

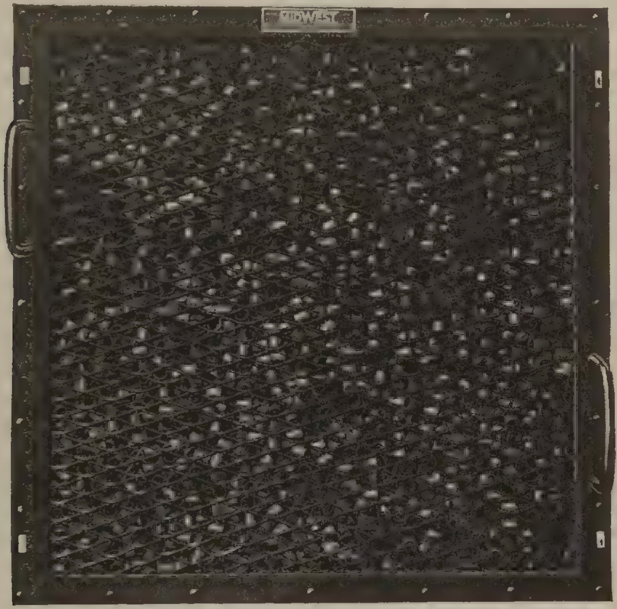


Fig. 244.—A single midwest air filtering cell removed for cleaning. The metal spirals which are covered with the viscose liquid to which dust and other foreign matter adheres, can be seen behind the wire mesh.

An air filter (Figs. 234, 244) made of wire cells filled with small metal spirals through which the air is drawn provides a means of removing all particles of dust without requiring power or much attention. The cells can be taken out, cleaned and charged with a viscose liquid. The special spirals are small metal cylinders with a comparatively large surface which is kept moist by the viscose liquid, and as the air passes through the filter bodies, particles of dust are brought into contact with the viscose liquid and cleaned through the adhesion of the dust. A tank for cleaning dirty cells and extra cells for use during cleaning are provided with the device.

Humidity Control.—Temperature is commonly regarded as the governing factor in determining the warmth or coldness of a room, but humidity plays as important a part in determining our comfort as temperature does.

Obviously, it is best to draw air for air supplies from above the building by shafts leading from the roof to the air washers and fans, but by the installation of an air washer or air filter, air can be taken closer to the ground if necessary.

Humidity is a relative term, meaning the relation of the actual weight of water vapor present in the air at a certain temperature to the total weight that it can hold in suspension at that same temperature. We know that the affinity of air for water vapor varies with the temperature.

For example: If we take outside air at 40°F., which has a relative humidity of 50 per cent., that is, it holds in suspension 50 per cent. of the amount of water which it can hold at 40°F., and heat that same air to 70°F., we can see that the actual weight of water vapor present will remain the same but the relative humidity will drop way below the original 50 per cent. because the air has been heated and its capability of holding water vapor has been increased. Right at this point is where we meet the difficulty in maintaining a proper relation between temperature and humidity. Air at 68°F., to be comfortable and healthful, should have a relative humidity of 40 per cent. To go below this point, to any extent, causes the room to feel chilly because the air is constantly taking moisture from our bodies, and to go above this point causes us to feel oppressed and drowsy, because the air cannot take up all of the moisture that our bodies, give off. It can easily be seen then how with a temperature of 68°F. and a proper relative humidity we may feel perfectly comfortable, whereas with a temperature of 75°F. and a low humidity we feel chilly.

Humidity control then is a matter of vast importance, especially in a hospital, and should, in a well-designed institution, be given consideration equal to that given to other equipment intended to promote comfort and healthful conditions.

The process of adding to, or subtracting from, the relative humidity of the air is known as "air conditioning" and is accomplished by what is known as a humidifier or de-humidifier. Humidifying the air is usually accomplished by heating the air to a certain calculated temperature and then passing it through a spray chamber which will cause it to become saturated at this temperature. It is then reheated and at the final temperature will have the desired relative humidity as controlled by the temperature at which it was saturated. De-humidifying air is not so simple a matter as it requires that we cool the air sufficiently to cause it to precipitate enough moisture so that when we reheat it, it will not have a relative humidity in excess of what we desire. The cooling process is usually accomplished by a cold spray chamber, the water of which must be cooled by some form of refrigerating element.

Both humidifying and de-humidifying apparatus can be designed to be absolutely automatic, continuously furnishing a predetermined condition of temperature and relative humidity irrespective of the outside air conditions.

Many places of amusement and restaurants have found that it pays to install air cooling and air conditioning apparatus, notwithstanding that the first cost is often very large; it attracts patronage in summer when outdoor conditions are almost unbearable and it has been proven that they have met a demand, and that large numbers of people acknowledge the benefits. It is manifest that the sick would also appreciate the grateful reviving relief of living in ideal air conditions, which are found outdoors in natural surroundings on a perfect summer day, i.e., clean, fresh, gently moving air of an ideal temperature and humidity.

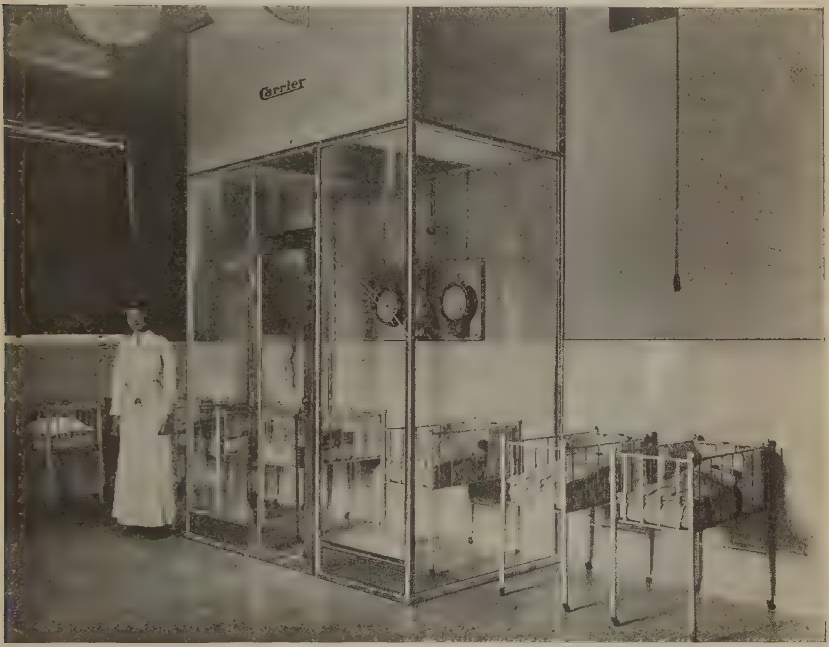


Fig. 245.—Apparatus for providing air of proper temperature and humidity for premature infants, etc.

Children may not take as much notice of humidity conditions as do adults, but it manifestly has a considerable effect on their mental condition, and proper air conditions unquestionably can be an aid, and probably are one of the most important factors, in combating diseases by improving the patient's physical condition.

Its cost of installation, however, is large and very few, if any, institutions will attempt to provide humidity control, with the possible exception of special rooms such as recovery and incubator rooms.

Would not every patient improve in such conditions? Would not his vitality be increased and every condition be improved and elevated to a more desirable level. It can unquestionably be done; the expense does not seem too great to attempt to provide such conditions in a hospital, and it is obvious that it should be provided for at least incubator rooms and that portion of the hospital set aside for the accommodation of patients subsequent to operations (Fig. 245).

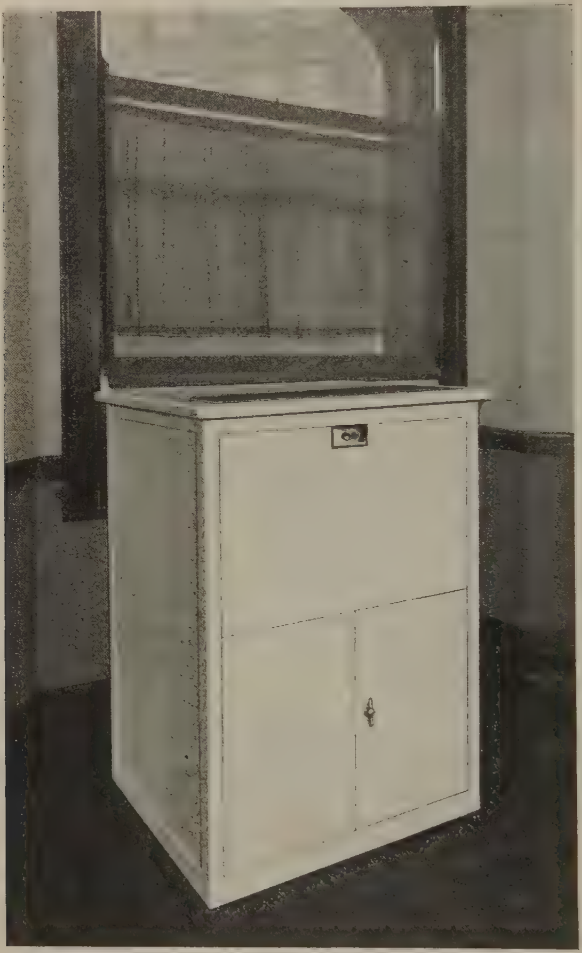


FIG. 246.—Univent ventilator cabinet.

Special Ventilating Units.—A univent or ventilating system in cabinet form has several good points, and can be used to advantage in special places. It has been developed to the point that it will do its work without noise or objectionable air currents. The one shown in Figs. 246, 247 has a capacity of 1500 cu. ft. of fresh air per minute.

This air can be taken in from the outside through a short inlet duct and is heated to 70 degrees by passing over a heating coil and arranged so that the temperature of the air is regulated by a thermostatic control of the dampers.

The fans discharge the air downward with considerable velocity directly over a shallow pan of water; dust, soot and other particles of foreign matter that are heavier than air, are projected into the water and clean air passes to the top of the cabinet and directly into the room.

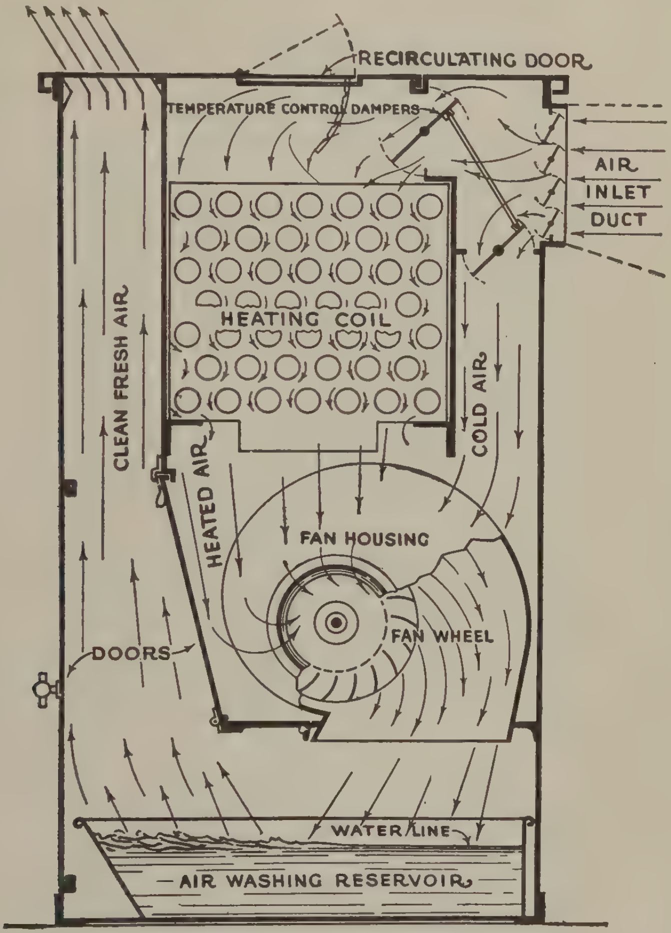


FIG. 247.—Section of univent ventilating cabinet.

The short inlet and discharge ducts make it possible to operate the univent cabinet by a ¼ hp. motor, very much less power than is required by an ordinary system of ventilation which has long ducts; further, it eliminates the annoying objection to the ordinary system of accumulating large quantities of dust in long ducts, when it is not in use and which is later blown into the rooms.

A system of this kind can be used when it is needed, and one part of the building can be supplied with fresh air without operating a large system that is expensive to install and operate. It is strange the amount of opposition that is raised against the use of univents by some engineers and ventilating contractors. They would rather take in air from the outside directly under the radiators, making an arrangement that is unsanitary, and exhaust air out of the room through an exhaust fan, than to use a system that can be made and completed in a factory, and deliver purer air than outdoor air.

Ozone.—Ozone and oxygen are identical, except that the ozone molecule contains three atoms of oxygen and the oxygen molecule two. It is produced by an electric current streaming or flowing through the air, and condensing or changing the oxygen into a more concentrated or more active form. Liberating a small percentage of ozone into a room the excess oxygen immediately oxidizes all germs, decaying vegetable or animal matter, and by this process it eliminates the formation of molds and odors, and maintains the air in a sterile condition.

By using a small portion of ozone, 0.05 part or less per million, great claims are being made as to its purification of air. Heating and ventilating engineers are using and making tests on ozone equipment. They claim a saving of approximately 50 per cent. in fuel in schools or assembly rooms, in which by using ozone a greater portion of the air required for heating the room can be re-circulated. Standard ozone units are now available, and the cost of operation is small.

The milk preparation room is hard to control and keep in a sanitary condition, for the material handled is a food and natural breeding place for germs.

The pasteurizer may do its work perfectly and still contamination may take place before the containers leave the room. A small ozone machine can be used to advantage in this department; it will eliminate all odors, produce a sterile atmosphere and make possible the production of sterile food.

Illumination.—Electricity has practically superseded all other forms of illumination in hospitals. The source of current is either from a public service company's lines or from a local power plant. Where the public service company's transmission lines are long there is a certain amount of risk that their service may be interrupted during storms. To eliminate the harmful effects of such an interruption if gas is available, emergency gas lighting outlets should be provided in the operating and dressing rooms.

In the service rooms, office portion and the portions of the hospital open to the public, the lighting to a considerable extent should be studied to conform and harmonize with the architectural treatments, and to the location of the furniture and equipment; lighting fixtures covering various standards of indirect lighting are available for this purpose. In the public service portions of the building a considerable range of selection is available, but no type of fixture should be selected which allows excessive glare. The private rooms and wards require in general the soft subdued lights and this will be accomplished when the so-called indirect fixtures are used. The indirect fixture has an inverted shade which throws the rays of light against the ceiling, from which they are reflected and diffused throughout the room. In the semi-direct lighting, the inverted bowl is made more or less semi-

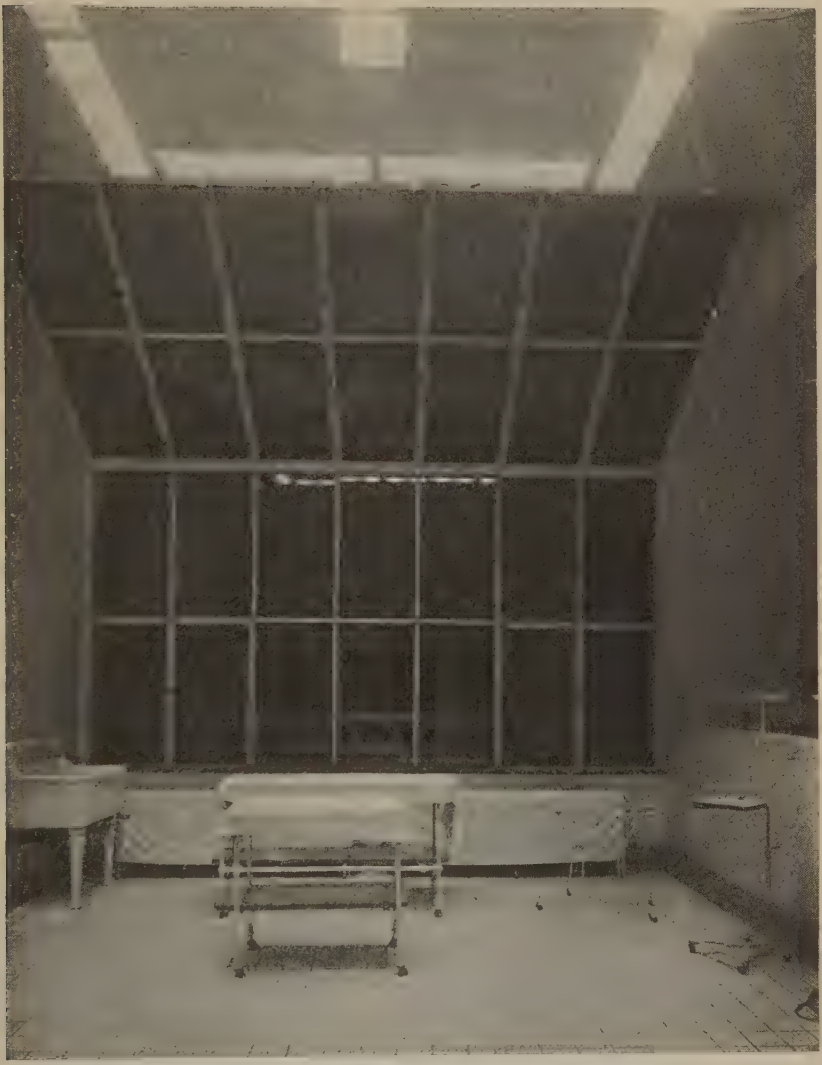


FIG. 248.—Photograph taken at night of one of the operating rooms of Cook County Hospital, Chicago, Ill. Flush concealed illuminating units; note absence of glare. (Richard E. Schmidt, Garden and Martin, architects.)

luminous allowing a portion of the rays to be projected downwards, the remainder being reflected from the ceiling as mentioned for the indirect fixtures. Side wall bracket lights can also be used to advantage in the private rooms and small wards in which case it is possible to eliminate the ceiling fixtures.

In conjunction with the bracket lights it is advisable to have an extra socket or special wall plug for connecting an inspection light. An additional plug outlet in a great many cases is advisable to which a portable or table lamp can be attached. Other electric specialties, such as electric warming pads, can be attached to these plug outlets. In selecting wall plug outlets for the children's hospital, it would be advisable to use flush receptacles having automatic closing shutters to prevent the children from being burnt by coming in contact with live electrical parts. The lighting of the operating rooms is the most difficult of hospital lighting problems. The light should correspond in direction, source, intensity and color as near as possible to day-light illumination entering through large north windows. The Figs. 241, 248, 249 show a combination of daylight and electric lighting of an operating room. Fixtures extending from an operating room ceiling located directly over the operating table have a tendency to gather dust, and for this reason are more or less of a menace in the operating room. The ideal lighted operating room would be one having a lighting distributed in such a way that the reflection and diffusion from the walls and ceiling would make it practically impossible to create shadows, by installing lights in the ceiling and side walls in a trough flush with the interior finish. The trough to be covered with a flush door con-

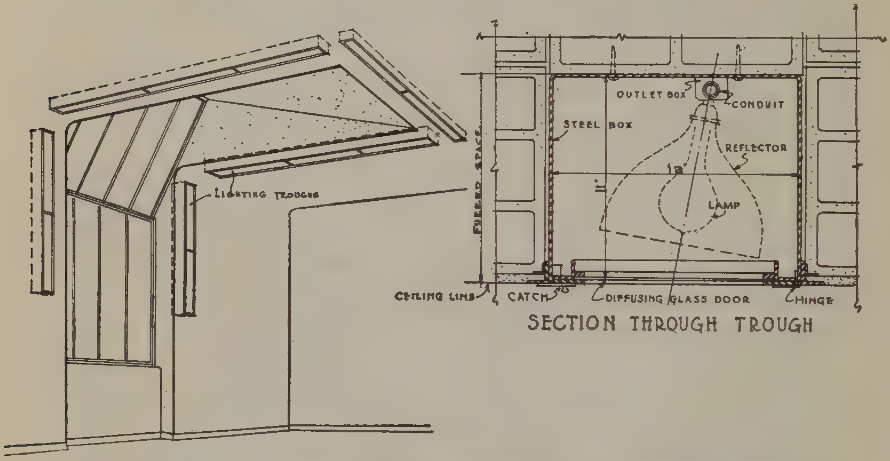


FIG. 249.—Special artificial lighting arrangement for operating rooms, consisting of steel troughs with doors glazed with diffusing glass flush with plaster, rows of adjustable reflectors. The direction of artificial illumination approximates the direction of daylight; the arrangement casts no shadow and has no projections to gather dust. Lower sash of two side sections of window should be hinged and screened.

sisting of high efficiency diffusing glass similar to Holphane glass. Each light to have a highly efficient mirrored reflector throwing the rays of light on the glass. The greater portion of this lighting should be from the ceiling, but there should be enough extending down the sides of the operation room windows to insure a strong horizontal diffusion of light at the operating table level. This type of lighting fixture being flush with the wall is easy to clean.

There are a number of ingenious and commendable operating room fixtures extended from the ceiling that are arranged specially to concentrate the light upon the operating table. Whenever this type of fixture is used, it is necessary in a great many cases to use spotlights, which can set on the floor and be connected by plugging into a wall receptacle in the walls of the operating room.

The lighting of an operating room should be arranged so that it can be controlled from several switches for only during the operation is the maximum amount of light required. In selecting incandescent lamps and reflectors, there are on the market so-called daylight lamps, and reflectors that give practically daylight conditions.

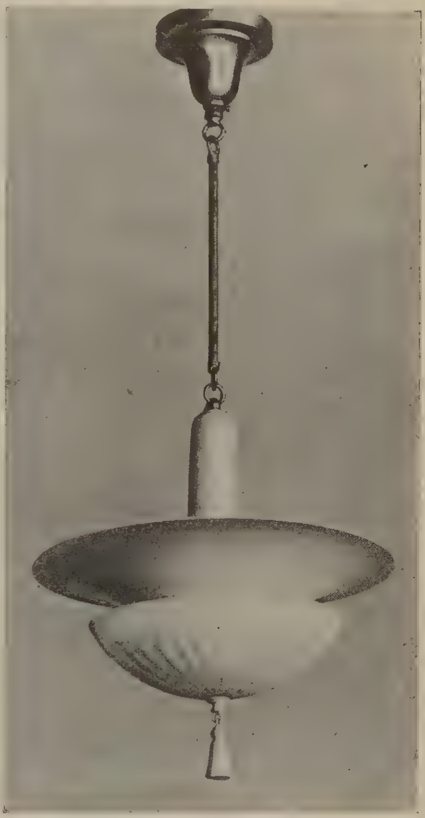
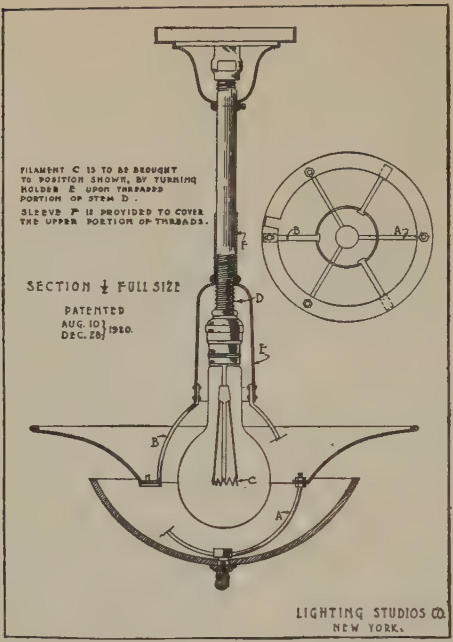


Fig. 250.—Semi-indirect ceiling fixture. Figure 249 illustrates the construction.

Children's senses are not so susceptible to badly placed artificial illumination, but it seems desirable to give them the benefit of the best forms of hospital illumination, *viz.*: ceiling fixtures can be obtained in which the strength of the light can be regulated as may be required (Figs. 250, 251). In these, as the room may require, different sizes of lamps, from the lowest to the highest wattage, can be used and adjusted to be in focus for maximum reflection without unduly increasing the percentage of light passing through the bowl.

In the private rooms and wards it is well to consider the installation of special night lights in order to disturb the patient as little as possible when the nurse visits the room. Experience has shown that by throwing ceiling or wall lights on suddenly, it has a tendency to startle patients and disturb their rest. In order to eliminate this,



FILAMENT C IS TO BE BROUGHT TO POSITION SHOWN, BY TURNING HOLDER E UPON THREADED PORTION OF STEM D.

SLEEVE F IS PROVIDED TO COVER THE UPPER PORTION OF THREADS.

SECTION ½ FULL SIZE

PATENTED AUG. 10 } DEC. 28 } 1920.

LIGHTING STUDIOS CO. NEW YORK.

Fig. 251.—Ward illuminating fixture. Adjustable to foci of lamps of varying candle power.

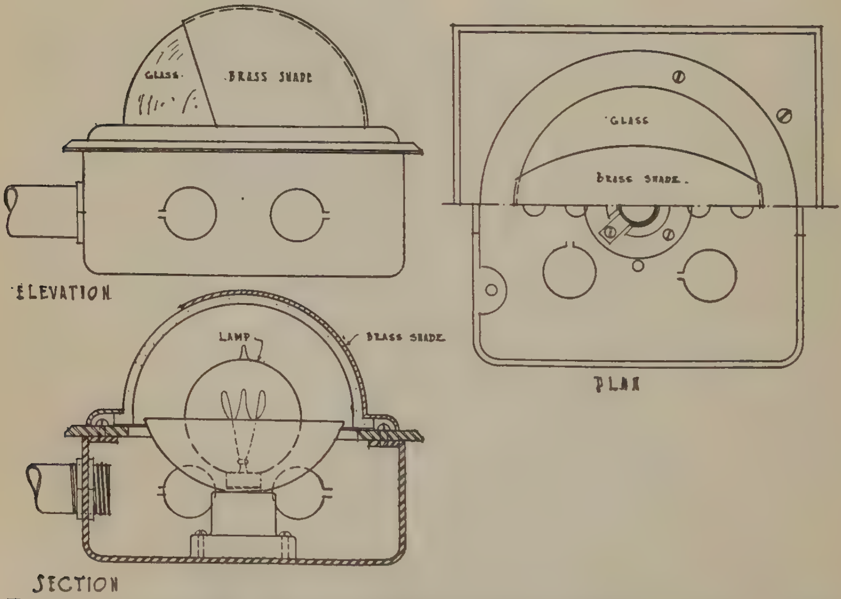


Fig. 252.—Fixed night light in standard outlet box located in walls or base boards, hemispherical globes and brass shades.

special night lights should be installed, preferably near the floor. These lights to consist of a small lamp having a bull's eye or dome shaped reflector, so placed that it will distribute light over the floor sufficiently to enable the nurse to visit the room, and not disturb the patient. These night lights should be designed so that they will not throw their rays on to the ceiling or directly on the patient's face, and should be located in the wall near the head of the bed. Lights of this type are shown in Fig. 252. The necessity of night lighting is

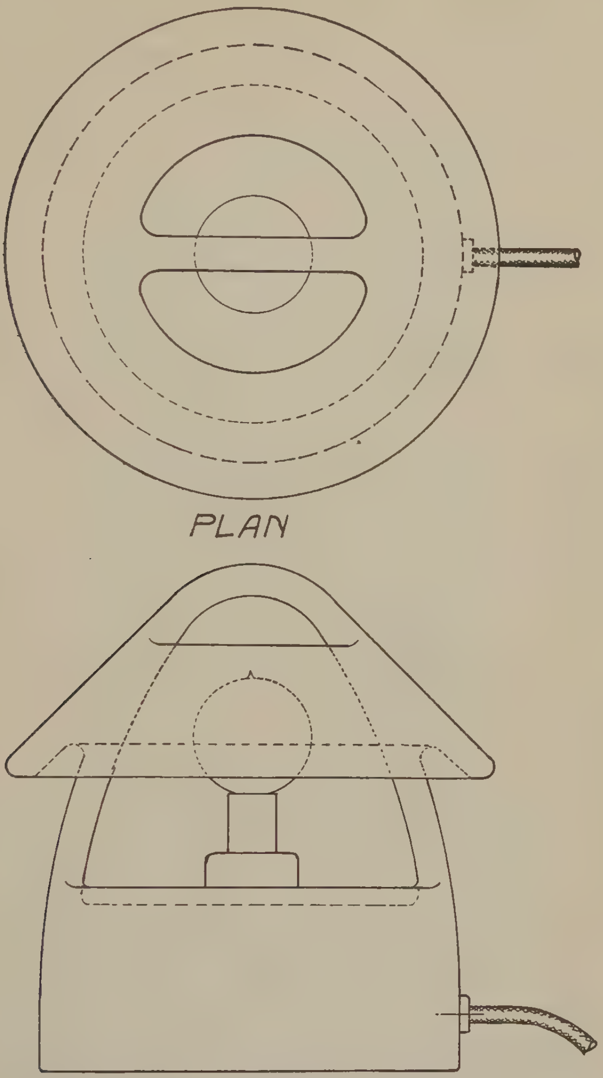


FIG. 253.—Portable night lamp of heavy brass, suitable for floor or table and dim illumination. Can be turned over or kicked without breaking.

borne out by the fact that a great many times ordinary lamps are placed under the patient's bed, or table or bracket lamps are covered with paper or another inflammable material. The use of small night lights reduces the amount of current consumed.

Lamp boxes sunk into the floor are in use but it is difficult to replace burned out lamps inasmuch as the heavy plate glass covers must be screwed down to make them watertight. Light boxes set above the base boards are more economical and illuminate only the floor sufficiently to allow a nurse to move about without danger of stumbling over furniture.

Figures 253, 254 illustrate substantial portable floor lamps.

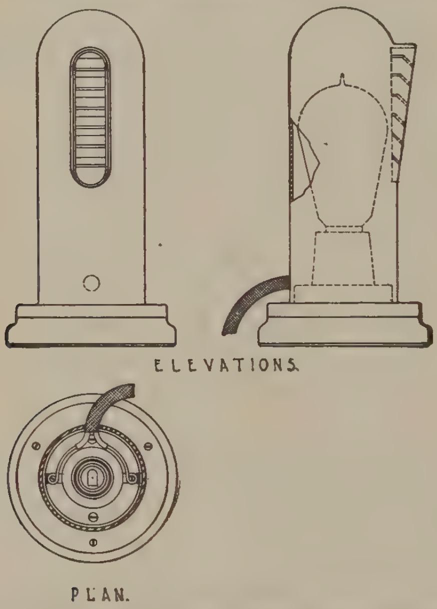


Fig. 254.—Portable night lamp of heavy brass, suitable for floor or table, illuminates dimly. Can be turned over or kicked without breaking.

Signal System.—If an electric signal system for calling nurses to the patient's bedside is considered essential, it should be of the noiseless type. The use of the common annunciator having a drop or target with a bell or buzzer to inform the nurse that a call is on is eliminated because of the noise. The signal system best adapted to hospital use consists of an annunciator, located at the nurses' station, which consists of a bank of individual low voltage lamps behind ground glass in a case set flush with the wall. When the patient pushes the button one light in the annunciator is lighted and the number of the room from which the call comes appears on the ground glass surface. This call stays on until the nurse goes to the bedside and presses the reset button. At the patient's bedside in the private rooms the signal system should consist of a flush plate over an outlet box, having a plug receptacle into which the patient's cord can be plugged. The patient's cord should be a heavy reinforced specially insulated flexible wire covered on the outside with a heavy braid. The push button must be strong enough to withstand severe use and be of simple plain design for sanitary reasons. The reset button should preferably be located in the plate on the wall, eliminating the necessity of the nurse handling the button the patient uses. In the case of wards a patient calling station should be located between each two beds, having two cords running from separate receptacles in the same plate, and in order to inform the nurse from which bed the call came in the case of large wards, a small bulls-eye light should be used. In order to facilitate affairs, all cords throughout the hospital should preferably be alike so that they are interchangeable and in case one cord is injured another can be substituted. In the majority of hospitals it is advisable to install over the door of each room or ward in the corridor a pilot light consisting of a small light covered by a dome shaped cover. This light to work in conjunction with the call at the nurses' station and is extinguishable by the reset button at the bedside. The use of these lights over the door saves the nurse many steps for she can observe these lights from any place in the corridor while on her various duties. Special pilot lights should be installed in the serving room, diet kitchen or in other work rooms, where the nurse's duties require her to spend a portion of her time. In order that she can tell that a call from the patient is recorded on the annunciator, these special pilot lights should be so wired that they will light up when any call comes in and stay lighted until the last call is canceled by the nurse at the patient's bedside.

A supervising nurse's annunciator can be installed in the superintendent's room which operates in conjunction with all other annunciators at the nurse's station. This supervising cabinet indicates the individual room from which the call comes and she can observe the time taken by any nurse on any of the floors to answer a call. Automatic recording devices are available that will record on a slip of paper the time it takes to answer any calls in the hospital. The use of the supervising annunciator or recorder in superintendent's office has a beneficial effect, for the nurse realizes a record of their unanswered calls is being made in the superintendent's office. A doctor's calling system is made of lamp annunciators located on various floors of the hospital and operated by push buttons located at the telephone switchboard. In case any one in or out of the hospital desires to communicate with a doctor, he calls over the telephone for the doctor. The telephone switchboard operator immediately presses the button corresponding to his number. The doctor upon seeing this on one of the annunciators goes to the nearest telephone and gets in communication with the telephone switchboard operator to find out where he is wanted, the operator in turn cancelling the doctor's call. There are systems of doctors' or internes' calls, consisting of buzzers or telegraph sounders mounted in the corridors on the various floors of the hospital and controlled by keys or buttons at the telephone switchboard. In the operation of this system the operator presses the button or key a number of times corresponding to the number assigned to the person called. The call is answered over the telephone as in the light system. The use of telegraph sounders has been quite successful and the noise does not seem to be annoying. The only absolute noiseless call system is the one depending for its operation upon the lighting of the lights. This has certain disadvantages for when the doctor is busy he is not likely to observe the light as soon as he would hear a sound.

Protection Against X-rays.—The *x*-ray machine in the last few years has been increasing constantly in power. The machines in use today are several thousand times more powerful then they were 20 years ago. These machines are so powerful that in order to obtain what is commonly called soft radiation filters are used for absorbing the rays of long length. The problem of suitable protection is becoming a serious one. It is not only a matter of 70,000 to 90,000 volts in action but 200,000 volts under three milliamperes. When we consider that in the case of recent cancer treatments which call for several hours of exposure to high intensity rays the question of protection must not only include the operator, but the other people in the building. The operator's booth should be protected by lead 1/10 in. in thickness, this lead being securely placed in the partitions or walls in such a way as to make a continuous lead shield; and it has been the general practice to provide lead glass observation windows through which the operator can direct the operation of the machine. Many *x*-ray specialists have been seriously affected by continued exposure to *x*-rays, and if the machines keep on increasing in power, the thickness of lead protection to the operators booth will have to be increased, and it may be found necessary to eliminate the lead glass windows and use the simple form of periscope instead. In order to protect the other occupants of the same building from harmful effects of stray *x*-rays there should be placed in the four walls and the ceiling an ample thickness of lead to safeguard their welfare. Lead sheets can be placed in the brickwork or tile with overlapping joints. and the lead in turn covered by furring tile and plaster. Lead exposed upon the wall mars the appearance of the rooms and in addition the expense of installation is high. In special cases where only stray rays are to be taken care of two or three layers of heavy lead foil can be glued on the walls or ceiling over which a layer of canvass can be pasted to receive the decorating. The use of lead foil will only be useful where the stray rays are weak; however it is a cheaper method than any other system of protection. Special care should be taken to have it applied properly. This also applies to any other system of lead protection, for the average workman does not realize what the protection is for and is liable to be careless in applying it.

A coating of a mortar containing one to four parts of commercial barium sulphate, one part of sand, one part of cement, applied to one or both sides of the partitions or walls of the x-ray room in the same manner as ordinary plaster, has been used in a few instances instead of sheet lead. The effectiveness of this material has not been fully established, however, it seems probable that a thickness of ¾ in. is equivalent to sheet lead $\frac{4}{100}$ of an inch in thickness.

It is important and necessary to have the barium sulphate uniformly distributed throughout the plaster.

Ventilating Windows for Dark Rooms.—Dark rooms can be ventilated through an outside wall or into other rooms and corridors by using one of the light-proof transoms illustrated in Fig. 223.

Telautographs, Teletypes.—Telautograph and the teletype are devices for almost instantaneous transmission of written orders and information from one to any number of other points. The telautograph, which transmits handwritten messages, has been in use for many years and is quite well known.

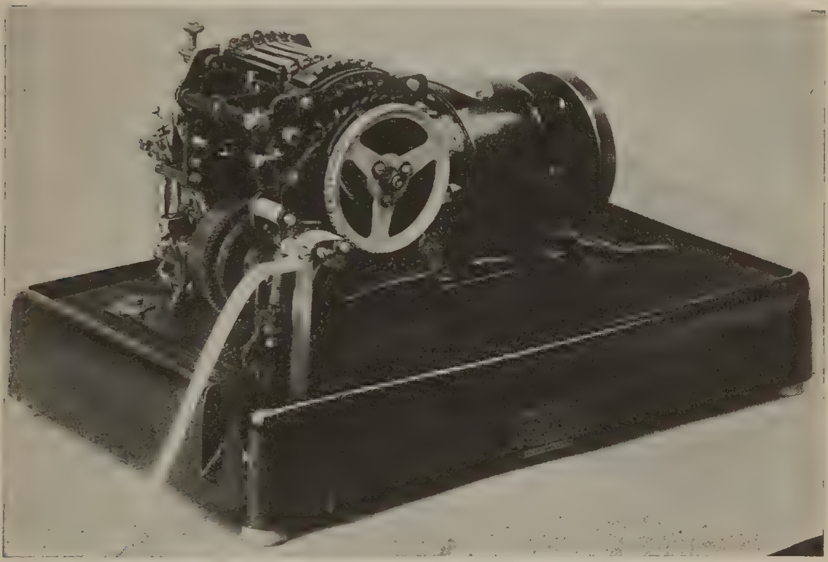


FIG. 255.—Printing telegraph instrument for receiving printed messages.

The teletype system consists of sending and receiving machines which will record what is being transmitted by means of typed letters and receive what is being sent to it on the same unit. The teletype machine (Figs. 255, 256) resembles a typewriter machine, which can be operated by anyone who can pick out the alphabet on the typewriter. It instantly produces typewritten messages on paper on any number of machines at any distance. Obviously, these are more legible than written messages and not as subject to error which may be due to illegibility.

Telegraphone.—The telegraphone (Fig. 257), a recent invention for the recording and transcribing of messages, seems a most useful addition to the equipment of a modern hospital. It records and reproduces the human voice or any other sound electro-magnetically on fine steel wire or thin steel discs. The same wire can be used indefinitely, or if desired the records can be preserved and read as long as the steel will last. Former records are automatically erased while new ones are being dictated on the same wire.

This appliance can be made of special service in expediting the record of clinical histories. The prompt, accurate and complete record of the history of every patient admitted to a hospital, and the subsequent entry of notes as to the daily progress of the patient is a *sine qua non* of good hospital practice. The writing of such histories is the duty and the privilege of the interne in every hospital where there are internes in service. Unfortunately, in a large proportion of these institutions there are no internes, and the history must be written by the attending physician. To record such histories in long hand is a laborious and time-consuming procedure. With the telegraphone installed in some room in the hospital far from the wards, where the noise of the typewriter may be entirely confined to the room; with the instrument, moreover, connected by telephone wires with each room and ward, so that connection with a transmitter may be plugged in at

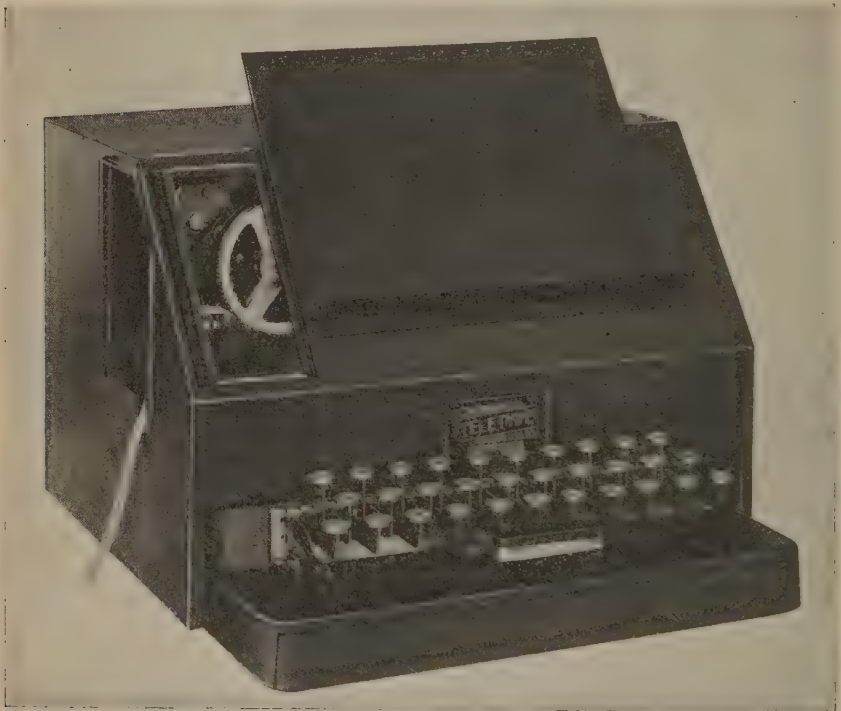


FIG. 256.—Printing telegraph instrument for sending and receiving printed messages.

convenient points in baseboard or wall; and finally with a transmitting advice similar to that worn by the telephone girl at the switchboard, supported from the shoulders or from a head-band worn by the physician, it is only necessary for him to dictate the clinical history as it is elicited from the patient or the parent, and as he proceeds with the physical examination and notes his findings, to "think out loud" in order to secure a permanent record in the distant receiving wire of the telegraphone. At her convenience, the typist transcribes the history on the typewriter and sends it to the room or ward to be reviewed and corrected by the attending physician at his next visit.

Experiments have been made in the making of records of heart and lung sounds which it is hoped will prove of practical use.

Elevators.—Reliable power driven freight and passenger elevator service is a necessity in all other than the cottage hospital. The use of long inclines or ramps as a means of eliminating the elevator has not proven satisfactory. The gradient is more tiresome to even a well person who is strong than a stairway.

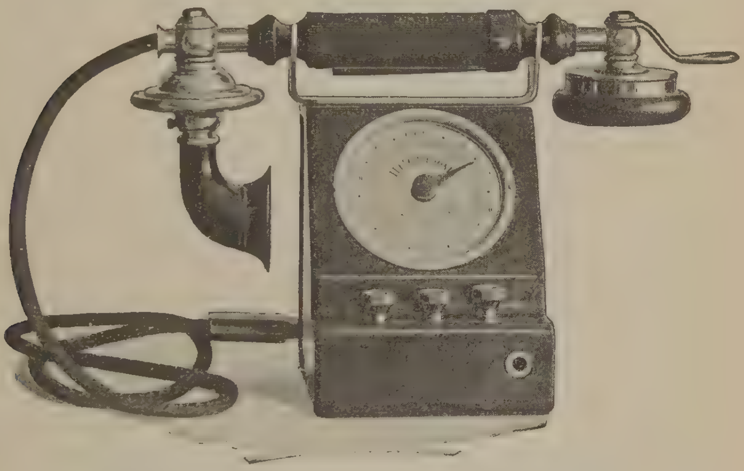


Fig. 257.—Telegraphone for recording messages, records, etc.

Most states and cities now have laws which require elevators in hospitals of several floors as well as for an inspection at regular intervals. The location of the elevators in the building is important to the best functioning of the service of any hospital and should have careful study by the designers.

The elevator selected should be of standard and trade designs as they are less expensive, both in installation, maintenance and for reliability of service, necessary for the functioning of a hospital. Repair parts may be more easily and quickly obtained at the least cost.

Electrically and hydraulically operated elevators are substantially the only types now being used as the steam elevator is practically passe. Hydraulic elevators have their place but are seldom used except for special service, kitchen or sidewalk lifts.

Electric elevators are known by two types. The drum type, which was used extensively until recent years, has a drum of sufficient capacity to receive the total length of cables. This type requires a set of counterweights and cables attached directly to the car frame and another set to the drum, both traveling in the same set of sheave wheels.

Traction elevators are practically superseding the drum type. In the traction type the cables are connected to the top of the counterweight and over main drive sheaves, then over an intermediate sheave in some cases and hitched to the shackles on the car frame. These cables do not wind up as on drum types, but are held by friction on the driving sheave. These driving sheaves are constructed of two types as indicated by their names, *viz.*, "U-groove" and "V-groove." The U-groove machines have cables passing over main sheave, around idler and back to main sheave to obtain the necessary traction force on the cables for the operation of the elevator. The V-groove traction machine is coming more generally into use. This consists of a main V-groove on the machine over which the cables pass but once.

Some traction machines built for direct drive are operated by having the driving sheave mounted directly on the end of the motor shaft and over the car, without gearing.

In selecting an elevator, one of the features that should not be overlooked is the brake. This must be strongly constructed, yet simple and of positive action. It consists of a band type clamp, by means of powerful springs mounted on the elevator machine base over a drum on the main shaft usually adjacent to the motor. The operative feature is made by a solenoid, which opens the brake when energized with current.

A few elevator machines have an additional brake on the drum shaft, which acts a little later than the first brake. The advantage of this is the added safety feature, and is especially commendable where patients are to be carried and gentle stopping is desired.

A capacity of 2500 lb. is usually sufficient for the average hospital elevator. The maximum speed should not be more than 150 ft. per minute and 125 ft. should suffice in buildings only two or three stories high.

Elevator machines are usually located directly over the elevator hatch in a pent house. The advantage is a lower first cost and lower cost of maintenance, the disadvantage being noise and vibration which is transferred through structural parts of building. To overcome this, special floor deadening construction under the elevator machine must be provided or else the elevator machine should be set in the basement, the latter requires doubling the length of cables and providing a heavy foundation, for adequately anchoring the elevator machine.

Essential to the electric elevator is the automatic control board, which is actuated through a special car switch, or push buttons in the car for the various landings.

Through this control board and electric limitation stops the car is prevented from traveling beyond the safety points at the top and bottom landings.

Where the passenger car is used for visitors a car switch control should be used, but if only employes, the push button control is satisfactory. Often it is desired to equip the elevator with dual control, that is, both the push button and car switch, which means that during visiting hours or at special occasions an operator is in charge of car; at other times the push button control is used, which change is accomplished by a special throw-over switch on the control circuit. A considerable saving in operating costs may be made by this arrangement.

Some trouble with accurate landings occurs with the push button control due to the load on the car and how much the elevator is used. Push button control should not be used for speeds over 150 ft. per minute.

One manufacturer has developed a machine which is known as the micro-leveling elevator. This has two parts, one a main hoisting machine, the other the micro-machine. With this micro-leveling elevator, accurate landings are made irrespective of the load and speed and it maintains this landing during the loading or unloading of the car independent of the stretch of the hoisting cables.

There is one special feature of this hoisting machine different from others which is the main brake, which instead of being bolted to the bed plate of the machine is fastened to the leveling device and revolves with it. This main brake performs a double duty: First, with the device at rest it acts as a brake to stop the main machine, second, with the device operating it acts as a friction clutch to drive the main machine. The leveling device in itself is a small elevator machine, consisting of motor brake and worm gear reduction, and requires its separate controller.

The operation of the micro-controller is accomplished through a leveling switch mounted on the car frame and has double contacts, one for up and the other for down direction. These contacts are operated by two stationary cams mounted at each landing. As the car approaches the landing at which a stop is intended, the circuit of the main motor is interrupted by either the floor controller or the car switch operating mechanism, and the leveling switch engages the hatchway cams, thus operating the micro-motor. The micro will then slowly raise or lower the car until it is level with the landing and stop the car.

The leveling switch is prevented from engaging these cams when the car passes the landings at full speed by a special magnet. When the power is cut off the main motor, this magnet is de-energized and if in the micro-zone, the leveling switch will engage the cam.

So noticeable in the hospital, where quietness is so essential, is the noisiness of some elevators, that in the selection of elevators special attention should be given each manufacturer's motor, brake and controller. Manufacturers have been making special efforts to build a quiet running, alternating current motor for elevator use. They have to a large extent accomplished the elimination of the hum of the alternating current motor, but the percentage of practically noiseless motors is small. One singular thing is that motors made under the same conditions in the same shop make a greatly varying amount of noise. Noise in connection with the electric brake is caused by a hum in the solenoid coils, due to a sudden application of the brake shoes to the brake pulley. If the brake takes hold too quickly the back lash in gears is quite noticeable.

On the control board, the magnets contain many moving parts, some of which are special carbon contact points for making or breaking control circuits. They will make some noise, which cannot be prevented and consequently should be isolated in a room separate from the hatch.

The hospital elevator cab should be given special consideration. It should be what is known as the sanitary hospital design, made of steel, provided with rounded corners and floor moldings so as to avoid sharp corners in which dirt can accumulate. The cab should be well ventilated, but care should be taken that not too much grille work is provided, causing excessive drafts when the car is in motion. The car should be finished in baked enamel, preferably French gray in color, and should be finished so that it can be washed down easily, Hand rails should be provided on all sides of the car. The car should be at least 7 ft. long and the minimum width of door 42 in. to allow for a stretcher or 48 in. for beds.

Two speed or two section doors are often required on account of space limitations, and they are also better than single doors of such large dimensions; only a strong, well-designed operating device should be selected for the doors of the enclosing shaft. Cheap devices are usually too flimsy to last long. Hinged doors in adjacent sides of elevator cabs located in the same shaft are very useful in emergencies. In cases where one car is caught between floors, passengers can be easily transferred to the other car. Hinged panels should be provided in the top of a cab of a single elevator, for this purpose.

Elevator Safeguards.—Many serious accidents, some fatal, have occurred because of improperly built or guarded elevators. In 1919 in one large city alone 34 people were killed by elevators.

Providing of safety devices on elevators and dumb waiters gives needed protection to employees and patrons against accidents due to the carelessness of the operator. Of these safety devices are door locks, both mechanically and electrically operated, which will not allow the opening of the door until the car has effected a landing within a given radius. As long as the door remains open or unlocked it is impossible for the operator to move the car in either direction, and further safety features are that no other shaftway door above or below may be opened until the car is brought within the landing range.

The electric door switch for breaking circuit is another device which prohibits the movement of the car up or down when the door is open or unlocked. If this type is used it is sometimes advisable to arrange an emergency switch in the car, under glass, so arranged that the car can be operated in event of fire or other emergency, even when doors are open.

In most service or freight elevators observations have shown that when doors are not closed, before the car leaves the landing, attempts are frequently made by persons to board the car before it gets too far away. It is then that accidents occur, usually by stumbling, which the operator is unable to prevent, for the operation of the brake on most elevators requires over a second to bring the car to rest.

Dumb waiters should be provided with a safety switch at the hatchway door to prevent starting of the car unless the door is closed. Signals should also be provided and so arranged to light when the car stops at the designated enclosure door, which should have a small glass panel for this purpose.

Automatic illumination, by special lamp fixtures of the threshold of the car door when the shaftway door is open, also is to be commended.

A car with two entrances is dangerous and objectionable, but if conditions warrant two entrances, a collapsible gate or sliding panel in the car should be placed on the entrance farthest from operator.

Horizontal sliding doors should not be used unless an operator is regularly employed on the car. Swinging doors are dangerous because they are likely to be left open, and because in closing they may push persons or objects into the shaftway, Semi-automatic vertical gates or doors are advisable for freight elevators, but the full automatic gate is a source of danger. It opens and closes as the car passes the floor and if anyone were to lean against or take hold of the gate he is likely to be injured or possibly fall down the hatchway.

The elevator cables are an essential factor in the safe operation of the car and should be periodically inspected. In most large cities, there are qualified city inspectors who pass on the condition of the elevator and cables. Cables of steel or "Swedish" iron are usually constructed of six strands of 19 wires twisted around a hemp core. An ordinary rule followed by many inspectors is, under average conditions, to condemn a cable when as many as five contiguous wires in a strand are broken.

Should records of the mileage made by a set of cables be desired, a suitable revolution counting device can be installed which will record the revolutions made in one direction and from this and knowing the drum size, the mileage travel may be computed.

Elevators vs. Dumb Waiters.—The merits of elevators as compared with dumb waiters, for efficiency in the distribution of linen, food, ice, trucks and other supplies from floor to floor and the return of soiled dishes, soiled linens and refuse should be based on the time required to furnish the service.

Dumb waiters meet the requirements of proper food delivery only when they are conveniently located to the kitchen and floor serving rooms, and the food is transported in containers to steam tables of the serving rooms and distributed from there.

If the food is placed on trays in the main kitchen or an adjoining general serving room, it is not advisable to use a dumb waiter if the food is expected to arrive at the bedside in good order, unless there is a battery of fast dumb waiters, say one for each floor; this will give good results if the trays are not allowed to remain too long in the floor serving rooms.

Dumb waiters also require a very careful placing of trays to avoid upsetting and breaking of dishes, which is a frequent occurrence in many installations. Soup and other liquids often spill and make a whole tray useless.

With an elevator, special food carts may be loaded with trays, taken directly to rooms without unnecessary re-handling of trays, and soiled dishes can be collected and returned to a central dish washing room in the same manner. This arrangement takes less of the employe's time in loading and unloading than dumb waiters require. Consequently with increasing speed and better service one or more trucks or carts can be carried on the elevator on each trip and distributed on the floors.

A small hand power dumb waiter is the best for quick handling of drugs and similar small and light articles.

Sound Proofing of Elevator Machine.—The disadvantage of setting the elevator machine placed on top of the shaft is, that without some kind of a noise absorber under the base of the machine, the operating noises will be trasmitted throughout the structure. To prevent this several types of sound absorbers of more or less merit have been tried and results obtained making an overhead elevator machine possible.

One of the means used to lessen the transmission of sound is to construct a secondary supporting concrete slab several feet above the top slab ordinarily used on an elevator hatchway, and so constructed that it is supported only by brick piers having sheet lead at base and top, the slab supporting machine to be entirely clear or free from direct contact with the exterior wall or partition, the mortar and lead joints absorbing and dissipating the vibration and operating noises.

As an additional safeguard a special concrete slab, floor or accoustic ceiling is sometimes placed under the deflector sheaves, where these are required. A ventilator in the pent house roof or walls also tends to dissipate to the outside atmosphere the disagreeable effects of vibration and noises.

Another means of largely overcoming the disagreeable effects of vibration is the use of a layer of highly compressed corkboard not less than 2 in. thick, of a density of 3 lb. per square foot. One way to use this corkboard is to bolt hardwood plank platform as large as the machine base to the floor, on top of which the corkboard is laid and on top of this another layer of hardwood planks which, in turn, is bolted to the lower layer of planks, and then bolt the elevator machine to the upper planks. Another method is to lay the corkboard directly on the fire proof floor, on this to construct a concrete base for the elevator machine and bolting it to the concrete base. Sheet lead laid under the base of the elevator machine will also assist in eliminating the vibration and noises.

Water Piping.—All water supply lines should have sufficient pressure to insure a reasonable flow of water at all times. In a great many cases pressure in the city mains is not sufficient to force water to the outlets in the top of the building, in which case it is necessary to install a tank and pumps to keep the tank full. The pumps should be automatically controlled by the water level in the tank, thus insuring a constant and uniform water supply. In a great many cases where the cost of coal or electric current is high, the cost of pumping is quite an item of expense. It is advisable to arrange the piping of the lower floors of the building so that the fixtures will be supplied with water direct from the city mains, supplying only the upper portion of the building from the house tank. This, however, increases the amount of piping to a considerable extent. The size of the cold water pipes supplying the fixtures should be carefully studied, especially if flushometer valves are used on water closets and clinic sinks. Hot water supply pipes, hot water re-circulating pipes and cold water supply pipes should parallel the waste pipes up through the pipe shafts or partitions of the building and as a general thing a special effort is made to have them fully concealed. These pipes should preferably consist of glavanized wrought iron, glavanized cast or malleable fittings and all branches to fixtures should preferably come out of the walls above the baseboard. Shut-off valves should for convenient control and repair be installed on each riser or group of fixtures. A separate system of pipes for fire protection should be installed and so located that water can be thrown into the extreme corners of each floor. In the majority of cases a 1½ in. hose is large enough to comply with local city ordinances. However, 2½ in. threaded valve openings may be asked for on the risers and in some special case 2½ in. hose may be required. Conditions may require the installation of a fire pump for the stand pipe system provided the pressure in the city mains is not sufficient. In the event that pumps are installed in the power plant, it is advisable in many cases to have them so arranged that by opening and closing of a few valves they can be used to pump water into the stand pipes.

Plumbing.—Plumbing pipes and sewers throughout the hospital should be cast iron or steel extending to a point outside the main building walls; from this point tile sewers can be used. Drain tile inside the building, for carrying away ground water, should be laid as required by local conditions. This drain tile should preferably be standard vitrified sewer tile laid with open joints and incased in broken stone. The tile should follow closely the exterior wall and have brick catch basins installed at every turn to facilitate rodding. At the point where the drain tile is connected into the main sewer a trap or basin should be provided. Special care should be taken to insure proper trapping in this basin in order to keep the drain tile free from sewer gas. In cities which have only one system of sewers and the storm water and sanitary sewage is carried through one system of drains, it is advisable to look carefully into the size of the system and the location of the building in relation to the sewers. In many cities the sewer system is too small to carry away a heavy rainfall, the sewer system in the streets fills and water rises and overflows into the street gutters. Unless some special provision is made to keep this water out of the hospital drains there is danger of water backing into the basement from the sanitary sewers, filling pipe trenches and other low floor levels, causing a very unsanitary condition to exist. In order to avoid sewers backing into the basement in a good many cases it is advisable to install bilge pumps which will not only take care of the surface water, but will eject the sewage from basement fixtures into the street sewer. The discharge of such pumps should always be provided with swing check valves. If the ground floor level of the building is close to the natural grade line, it also may be advisable to carry the drainage from the first floor fixtures through the pumps.

In cities which have a separate sanitary sewer system, independent of the storm water sewer system, the danger from sewage backing into the basement is generally caused by stopping of the sewer system and is of rare occurrence. Rising waste pipes should extend up through the building, preferably through ample pipe spaces with short branches to the individual fixtures. The number of the risers depends to a large extent upon the distribution of the fixtures and as a general thing it is preferable to have waste pipes vertical than horizontal. A large number of risers with short connections to the fixture is more efficient than a few risers and long horizontal branches in the floors and ceilings. The stopping up of plumbing pipes in the majority of cases occurs in the horizontal branches and wherever long horizontal branches occur, rod out plugs should be installed so that the house plumber can rod out the line.

Revents or ventilating pipes extending from each fixture or each group of fixtures should follow the main lines of the vertical drain stacks and extend through the roof. These should be large enough to prevent the syphoning of any of the fixture traps which would allow sewer gas to enter the rooms through the fixture waste.

In the modern hospital, appearance and sanitation require that all plumbing pipes be concealed in walls, shafts or partitions. The material generally used in this work is cast-iron pipe and fittings having caulked joints or cast-iron fittings and screw pipe using steel or wrought-iron piping. Wrought-iron pipe should be given preference over steel pipe, for it does not corrode as fast and consequently it has a longer life. Laboratory wastes should be run in salt glazed tile sewers, extended through the building walls and into the city sewer connection beyond the iron sewer. Special salt glazed traps are on the market for trapping such wastes and similar connections can be obtained for fixtures. As a general thing the actual connections to the fixtures are made by short pieces of lead pipe.

The arrangement and sizes of sewers, soil and waste pipes and ventilation piping follow the general practice required for other types of buildings and is governed largely by local rules and regulations; most of the cities permit the use of either extra heavy cast-iron soil pipe or galvanized steel or wrought-iron pipe for this purpose and where this is the case, steel or wrought-iron pipe with drainage fittings usually work out to the best advantage in connecting up to fixtures.

The water supply is an item that most local rules and regulations do not touch upon. A pure and abundant supply is obviously an essential. Lead or tarred cast-iron water piping is generally used for underground water supply pipes, and galvanized steel pipe or galvanized wrought iron is used for piping above ground. The water in certain localities may make the use of brass pipe advantageous, especially for hot water, but there are few places where this is a matter of necessity. For sterile water piping, of which there is considerable in the modern hospital, galvanized iron pipe lined with block tin has been found to give the best service.

Filters.—As a rule it is a good practice to provide water filters to filter the entire supply used in a hospital. Various types of filters are on the market for this purpose, but the type most generally used and which for convenience of installation and simplicity of operation seems to recommend itself as best adapted for the purpose is what is known as the pressure type quartz filter. These filters are closed steel tanks containing a depth of three or more feet of crushed quartz or quartz sand graded as to size. The water is introduced into the filters above the top of the filtering material and is collected through a system of branch pipes or arms and special strainer valves so distributed over the entire area of the bottom of the filter that the area of the entire filter bed is thereby made equally effective. The filters should be so proportioned that ample space for a considerable volume of water is allowed above the top of the filtering material and access manholes should be provided for draining and repairs. These filters for convenience in operation are generally installed in two or more units and cross connected by a system of pipes with valves so arranged that the supply to the filters can be reversed and the filters washed out, the water from the filters then discharging directly into the sewer.

Water Softeners.—Water softeners are required in many hospitals, on account of the hardness of the raw water supply. Where only hard water is to be had it is usually the practice, on account of the expense, to soften only a portion of the water, such as the water used in the laundry, main kitchen, and heating boilers, or sometimes the entire hot water supply is softened but not the cold water supply. Water softeners are of various types; one of the well-known types depends on soda ash as the principal agency of its process. Within the last few years another type of water softener has been introduced known broadly as the Zeolite type, which is a special mineral material used as mined and has properties which change the composition of the water. The softening properties of this latter type are restored from time to time by the addition of mineral salts.

Water Sterilizing.—Sterilized water is required in hospitals in connection with the operations in the operating room, birth room, in the surgical dressing and other rooms.

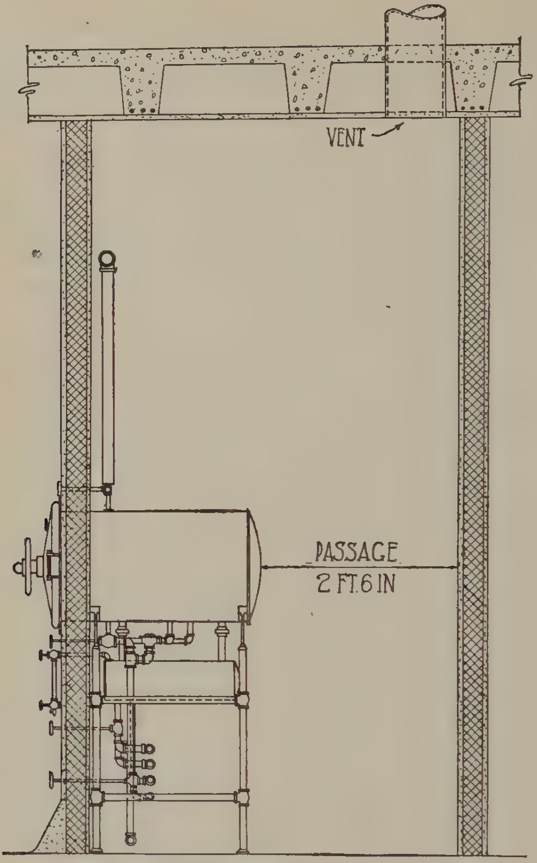


FIG. 258.—Concealed sterilizing apparatus. A cross section of a chamber for sterilizing apparatus sufficiently large to afford a convenient passage for inspection, repairs and adjustment. Only the doors, operating valves, gauges, cocks and thermometers project through the wall between the chamber and the sterilizing room. This arrangement reduces to a minimum the heat radiating surfaces exposed in the sterilizing room, also the area of polished metal, consequently the arrangement not only results in comfortable temperature conditions in the sterilizing room, but also reduces the labor of polishing. If desired escaping steam and heated air can be drawn from the chamber and passageway by ventilating fans.

In order to insure sterilization of the water, most authorities agree that the water should be subjected to a heat temperature of 235 to 250°F., for a period of 15 minutes or more.

There are two general methods for accomplishing the sterilization of water. One method is to have a central sterilizing plant, generally installed in some room in the engine room or basement of the hospital, consisting of a series of tanks containing pipe coils with high pressure steam connections severally properly controlled by automatic regulators, in order that the water in each tank should be of the temperature desired. One of the tanks is used to heat the water sufficiently for sterilization, another tank to cool the sterilized water, a third tank to store hot sterilized water of proper temperature for use in the building, and a fourth tank to store a supply of cold sterilized water, also for use in the building. From this central battery of tanks hot and cold water supply pipes are installed to the various rooms in which the sterilized water will be required, and is drawn through faucets in these rooms. The hot water supply piping is arranged in the form of a loop to insure constant circulation and a constant supply of hot sterilized water. All piping in the system should be block tin lined pipe and the coils in the tanks should be of copper or brass properly tinned.

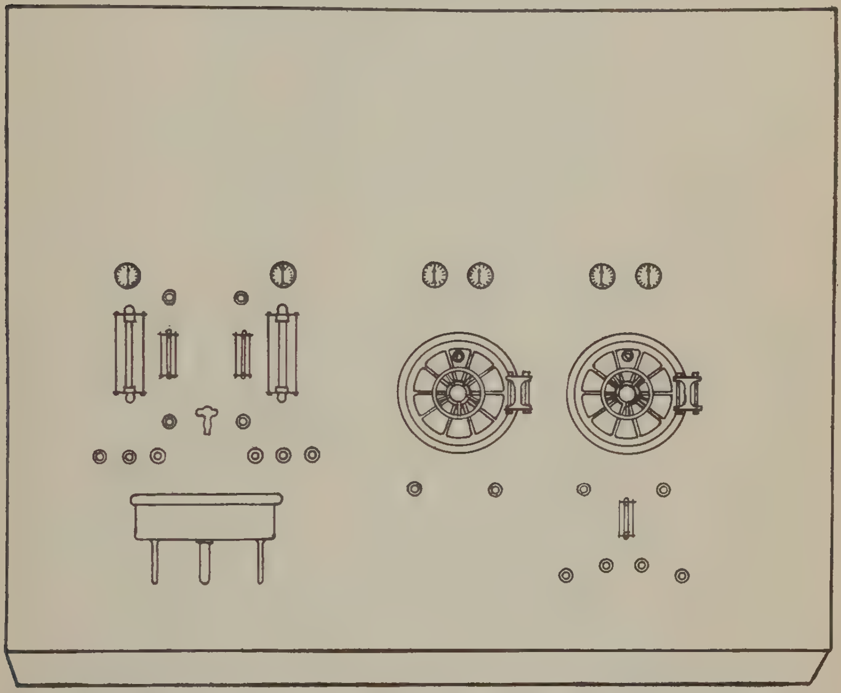


FIG. 259.—Concealed sterilizers. Elevation of wall of the sterilizing room through which the doors, thermometers, cocks, valves and gauges protrude. Note the concealment of large areas of metal surfaces and pipe.

A second method is to have sterilizing water units in each location where sterilized water will be required. These units are in small sizes and are manufactured by many of the hospital supply companies. The water in this case is drawn directly from the sterilizing units. These small units are generally of tinned or nickeled copper and are installed in batteries of two tanks, one for hot and one for cold water. The heating element to produce the sterilization in these small units may be steam, gas or electricity.

In some cases where central sterilizing plants are installed, the water is re-sterilized again by one of the smaller units just described before being used, making double sterilization.

Plumbing Fixtures.—The plumbing fixtures for a hospital are quite varied in their character on account of the many different uses which they serve and many are required which are specially designed for this type of building.

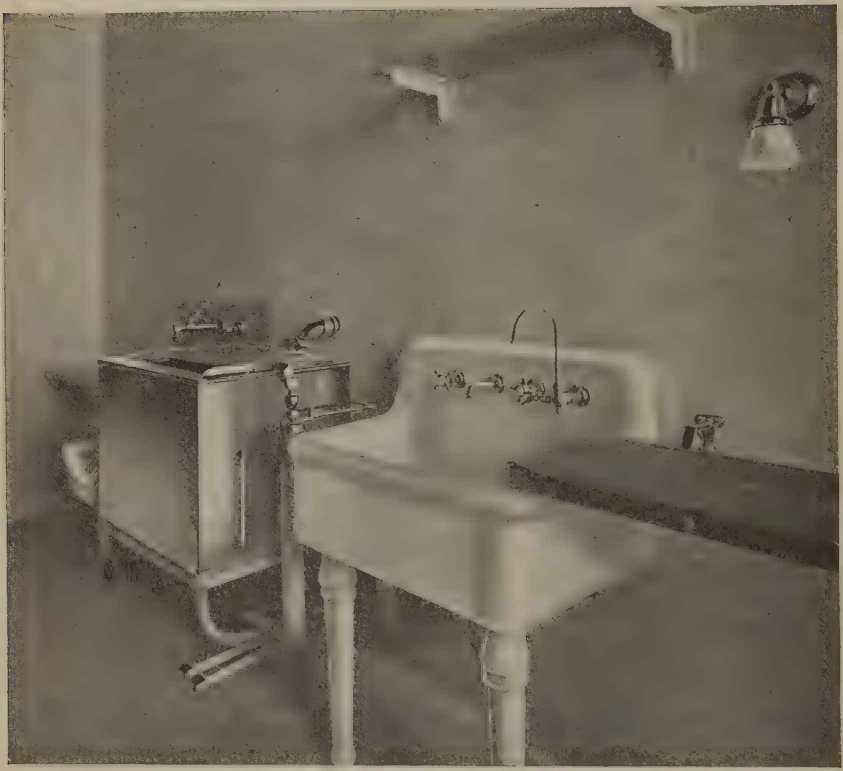


Fig. 260.—Utility room equipment, Illinois Central R. R. Hospital, Chicago, Ill. Wall hung clinic sink and utensil sterilizer sink, folding drainboard and marble shelf. (Richard E. Schmidt, Garden and Martin, architects.)

Water Closets.—Water closets of standard type with projecting lips are generally used. A closet as nearly noiseless as can be obtained should be selected. Seats of some hard composition, impervious to water, are recommended over standard wood seats.

In many cases wall hung closets can be used and are preferable to those standing on the floor, inasmuch as they facilitate the cleaning of toilet rooms; they are, however, more noisy and require a strong water pressure for their operation. Where installed they should be used in connection with flushing valves.

Slop Sinks.—Urinals, slop sinks and the general room lavatories are of same type as used in other buildings. Where lavatories are installed in doctors' examination rooms, nurses' work rooms and surgical dressing rooms, they should have knee acting or elbow acting supply valves.

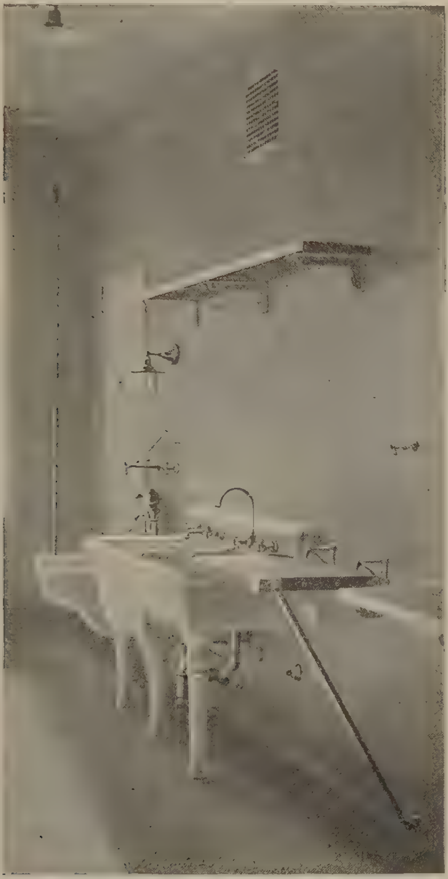


Fig. 261.—Utility room equipment, Illinois Central R. R. Hospital, Chicago, Ill. Wall hung clinic sink, combination laundry tray and sink, folding drain boards and marble shelves. (Richard E. Schmidt, Garden and Martin, architects.)

Utility rooms should be provided with a clinic slop, a utility work sink, a bed pan sterilizer, and a gas or electric hot plate and a small refrigerator (Figs. 260, 261).

The clinic slop sink may be of the standard type of vitreous hospital clinic sink; it should have a flushing spout for cleaning bed pans. The work sink may be of two types. In Fig. 260, the arrangement usually installed is shown, *viz.*, a porcelain sink of kitchen type with a back in one piece and wood drain board arranged with hinges and a telescopic leg, so that the board can be folded back to the wall when not in use for convenience in cleaning.

A second type of work sink is shown in Fig. 261, which consists of a combination sink and laundry tub; this serves all the purposes of the other type of work sink and in addition has the laundry tub in which certain classes of soiled linen or clothes can be cleaned. It is especially adapted to utility rooms in connection wth children's wards.

The bed pan sterilizer is usually of the standard type; the cover should be controlled by a hydraulic lift operated by a foot pedal.

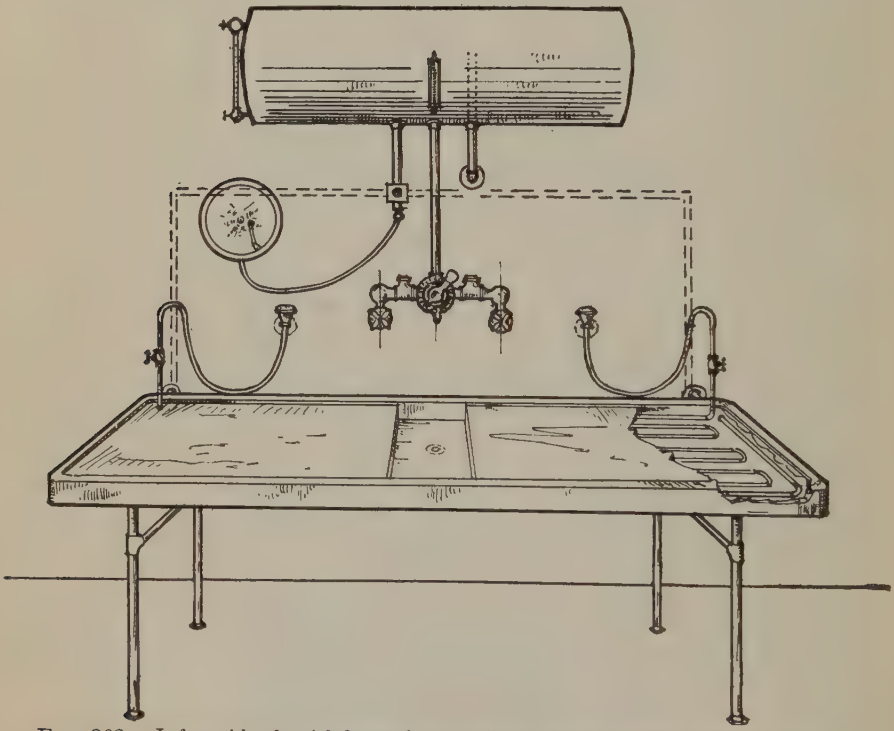


Fig. 262.—Infants' bath with heated top, mixing valves, storage tank, recording thermometer and rose sprays.

Continuous Baths.—Many hospitals have one or more continuous flowing baths for certain treatments. These are usually of the standard type, designed for this purpose, and should be set free from walls, so as to have an unobstructed working space all around the tub. A good plan is to omit the legs on these tubs and have them set on a special raised base 6 or 8 in. higher than the general floor. The water supply to these tubs should be controlled by thermostatic valves of the best type so designed that only water of the desired temperature can enter bath tub.

Infants' Baths.—Infants' baths require a special fixture for this purpose. Several of the standard plumbing supply houses illustrate fixtures designed for this purpose. In general they consist of a sink with a drain board or slab at either side, all made in one piece; a supply tank set up above the sink, with hot and cold water connections, with shut-off valves, thermometers and connections for a hose spray. The operation consisting in filling the tank with water of the proper temperature, then shutting off the tank and bathing or sponging the infants with the water in this tank until the water is exhausted when a new charge of water is introduced into the tank. In most of the standard types no provision is made for heating the slab on which the infants rest to the proper temperature and holding it at this temperature. To overcome this difficulty, in one of the institutions designed by the author a children's bath was designed as shown in Fig. 262.

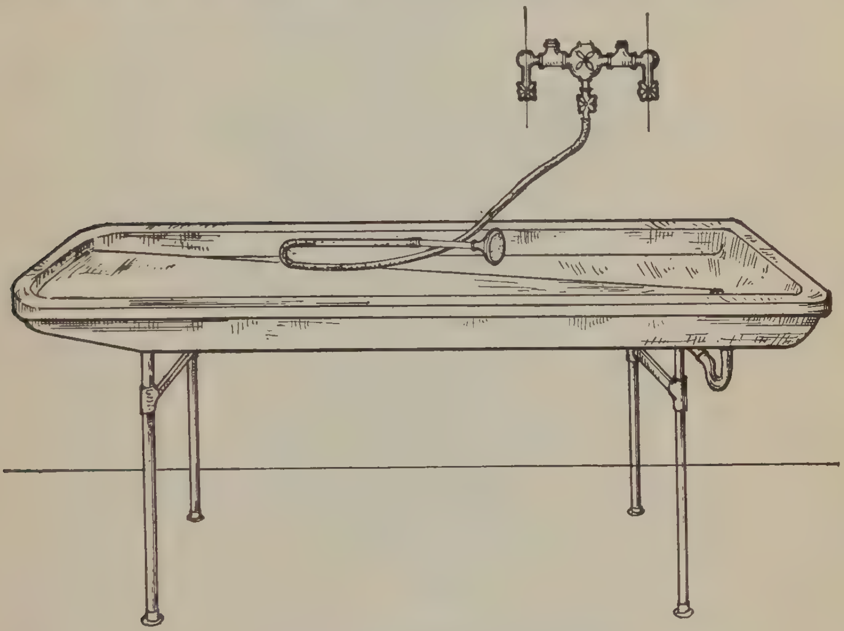


Fig. 263.—Receiving bath with rose spray.

This was constructed of German silver, the bathing slabs being a hollow compartment in which a system of circulating pipes was installed, and the space between the circulating pipes and the compartment walls filled with iron filings. The water from the tank passes through the circulating pipes and is then used through the spray nozzles, thus bringing the temperature of the slab to approximately the same temperature as the water that is being used. This has been used for several years and has given good service.

Receiving Bath.—Another special bath fixture required in most hospitals is the receiving bath. Figure 263 is a tray bath which is well adapted for this purpose. This bath is a shallow dish-like bath about 4 in. deep, 6½ ft. long and 30 in. wide with drain at one end. It may be made of porcelain or enameled iron. The tray should be set so that its top is 28 to 30 in. above the floor. It may be supported on pipe standards or porcelain standards, and should be set so that the attendant can work all around the tray. The supply fixture is generally set on the wall at one side with hose spray attachment. Temperature control valves are used on the supplies. Enameled iron is not as durable as porcelain but it does not require as much hot water as a porcelain bath to raise it to a proper temperature before using it.

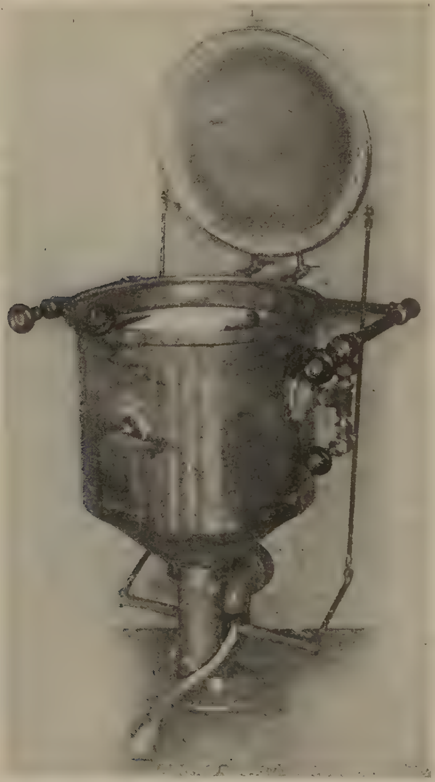


Fig. 264.—Bed pan washer and sterilizer. Almost every manufacturer of hospital apparatus and many hospital superintendents have designed apparatus to relieve the hospital personnel from the disagreeable work of cleansing bed pans. Several devices have been on the market which work more or less successfully; the device illustrated in the cut has been the most successful. After placing the bed pan in the holder and clamping the lid into place the pan can be revolved against strong sprays of water. The water escapes by continuous flow through the trap, and the walls of the apparatus are flushed from the hollow rings at the top of the tank. After the bed pan has been flushed and cleansed it can be sterilized by steam.

Bed Pan Cleansing Spouts.—In hospitals containing many single bed rooms with attached toilet rooms, it is a great convenience to have a bed pan cleansing spout at the side of the water closet. This saves time and travel of the nurses to empty the bed pans. These cleansing spouts are usually set a little above and at one side of the closet, and consist of a combination hot and cold water supply cock with long swinging spouts arranged to that the spout when in use can discharge over the center of the closet, and when not in use can be folded back to the wall.

Dark Room Sink.—A dark room for developing *x*-ray or ordinary photographic plates is considered an essential in all hospitals of any size. These dark rooms are equipped with a sink for developing plates. The sink should be of soapstone or some other acid-proof material, and should be divided into compartments to hold the various solutions required in the developing process. A good practice is to make these sinks 20 in. deep and 20 in. wide by 24 in. to 30 in. long on the inside. This will allow ample space for standard. A center supply cock with long swinging spout should be installed with this sink so that any of the compartments can be filled or washed out.

General Plumbing Rules.—As to general rules in connection with plumbing fixtures in a hospital, two fundamental objects should be kept in view.

First, to keep the floors of toilet rooms as free from obstructions as possible, making all fixtures as far as practicable wall hung fixtures, this for convenience of cleaning floors.

Second, to make the fittings in connection with fixtures of a material that will require the least amount of labor to maintain proper appearance. With this object in view as little nickel plated brass work should be used as possible. Constant polishing will destroy the nickel plating. White metal fittings have an advantage over nickel plated brass for this reason. Porcelain fittings are easily cleaned and should be installed wherever possible.

Refrigeration in Hospitals.—The use of mechanical refrigeration is today a standard equipment of hospitals of 75 beds or larger. The advantages to be gained are that the refrigerating boxes are a great deal drier, and the temperature of the individual boxes can be regulated to any desirable degree by opening or closing valves. It eliminates the tracking up of the corridors and stairs due to dripping from the ice while it is being distributed to individual refrigerating boxes. It is far easier to keep the boxes in a sanitary condition and the depreciation of the boxes is considerably less than where ice is used. The condensation from ice keeps the atmosphere in the refrigerator boxes damp, causing the wood to rot and metal to rust, and it could be safely said that the average stock refrigerator will last twice as long when mechanical refrigeration is used, compared to its life when ice is used.

In order to accomplish mechanical refrigeration, it is necessary to select some material for the refrigerant that will boil below 32°F. There are available quite a number of materials of this kind, but the ones most generally use are anhydrous ammonia or carbonic gas (CO_2). It is not advisable to locate an ammonia machine in a hospital, but where it can be installed in an adjacent power house, it can be used with perfect safety. The CO_2 machine can be placed in the hospital or in the power house, for the reason that the gas is an odorless non-corrosive material, and is not considered dangerous where there is a fair degree of ventilation.

The cooling of the various refrigerating boxes can be accomplished by what is generally termed direct expansion, or the boiling of the refrigerant gas in the expansion coils located in each box to be cooled. In most cases, however, it is found more advantageous to use what is called the brine system of cooling, and in turn cool the brine by expansion coils enclosed in the brine cooling tank close to the refrigerating machine. By making the brine tank a little larger, it serves both for brine storage and an ice freezing tank by making it large enough to hold a number of cans in which to freeze the ice required for special purposes about the hospital, such as ice packs, table use, etc. The cooled brine from this tank is generally circulated throughout the hospital by installing either an electric or steam driven brine pump. These pumps keep the brine in constant circulation maintaining a standard temperature in the various refrigerating boxes. In order to cool drinking water, a brine circulating coil is generally installed in the drinking water cooler. This brine is kept in circulation by the same pump that circulates the brine for the boxes.

The refrigerating machine can be either steam or electric driven, the choice of which depends upon local conditions. As a general thing, it is advisable to use a steam driven unit, for the simple reason that the exhaust steam effects an appreciable economy if used for the heating of water for domestic purposes, and when used in conjunction with the brine system, a large machine should be installed which would be operated only 8 or 10 hours a day when the hot water load in the hospital is greatest; a combination of this kind provides the most economical refrigerating system.

Insulation for Refrigeration.—Cork is the most effective insulation obtainable and is used in two forms. Granulated cork held in place by wood sheathing can be used in special places. As a general thing cork boards or special forms of cork sections are preferable. In forming this type of insulation the granulated cork is pressed in a special mold and when subjected to considerable heat, the natural rosin in the cork acts as a binder and holds it in the form desired. When cork insulation of this type is cemented around pipes or on walls and made air-tight, we have an insulation that is least affected by moisture. In a great many cases built up insulation is used, consisting of two or three layers of hair felt or wool felt, having canvas or pitch between each layer and the exterior covered and sealed by using several layers of pitched felt and canvas. A built up insulation of this type is effective as long as it can be kept dry.

The thickness of the insulation can be varied in accordance with the temperature of the brine that is to be carried through the pipes.

In the case of cork, standard thickness as made by the insulating manufacturers is adequate for hospital use.

Uses of Refrigeration.—Refrigeration in the hospital is used for cooling the refrigerator boxes which are generally located in kitchen and diet kitchen and used for cold storage and the preservation of food. In addition, small refrigerators are generally used in connection with the laboratory for preserving specimens, in the morgue for cooling the body boxes, and also for refrigerating special garbage storage rooms for preventing decomposition of the garbage until a proper disposition can be made of it. Cooling of drinking water and the freezing of ice are additional advantages to be obtained by using mechanical refrigeration.

In the hospital where all the boxes are cooled by mechanical refrigeration, there is a use of ice amounting to approximately 3 lb. per patient per day for the winter months and 4½ lb. per patient per day in summer months for use in ice packs, table use and special ice applications. Taking into consideration economy, cleanliness and comfort of patients, we find today practically every modern hospital equipped with mechanical refrigeration.

Milk Department.—An ideal milk preparation arrangement would consist of three rooms, one room into which all utensils, bottles, etc., are brought after being used. In this room the utensils and bottles should be washed, sterilized and dried before being taken into the work room. Such a room might be called the "uncleaned dish room."

Another small room located preferably adjacent to the first room mentioned should be provided to receive the milk as it comes to the hospital. A refrigerator compartment opening into this room would be a great aid in storing and preserving the milk, until such time as it is ready for further treatment. This room to contain a small work table, a pasteurizer, sink and untensil sterilizer, and can be called the "unpasteurized milk room." The third room or main work room should be large, light and properly ventilated, the pasteurized milk to be taken into this room as soon as it is pasteurized, and stored in the large refrigerator. The sterilized bottles, their containers and utensils, after proper cleaning in the uncleaned dish room, should immediately be brought into the work room, clean, sterile and ready for use.

Milk Room Equipment.—The uncleaned dish room should preferably contain two sinks for washing bottles and utensils. In one compartment of the sinks, a series of hot-water jets are provided to wash the inside of the bottles. Large drainboards on each side of the sinks. A bottle sterilizer and a utensil sterilizer of standard make will sterilize the bottles and utensils. If properly handled, one large utensil sterilizer will do all of the sterilizing work required in this room. A hot plate equipped with a drying oven on one end is quite essential.

In the pasteurizing room, or unclean milk room, there should be a large sink with a full size drainboard and pasteurizer, hot plate and a utensil sterilizer. To this should be added a refrigerating storage box for storing the raw milk as it enters this department.

The pasteurizer is the means of heating the milk from 140 to 180°F. and holding it at this temperature from 30 to 40 minutes. There are quite a number of pasteurizers on the market in which a high temperature steam coil comes in direct contact with the milk to be pasteurized. This type of pasteurizer has a tendency to overheat the milk adjacent to the coils and an agitation of the milk is necessary to obtain the desired result. A simpler form of pasteurizer can be used and is comparatively inexpensive to build. This can best be accomplished by using a standard Bain Marie, equipped with a steam coil in the bottom and controlled by a standard thermostat that will control the temperature of the water within a range of one or two degrees. The milk to be pasteurized should be put into small containers of metal or glass that are submerged in the water. Special vented tops should be provided for these containers, to project above the water line, in order to permit the contents to expand. A utensil sterilizer of standard make should be installed to sterilize the containers, tops and utensils. This room should be provided with a standard size hot plate, which can be used to advantage in this room. The attendants can prepare on this hot plate special foods, etc., which can be carried on in conjunction with the pasteurizing, which must be under continuous observation. In the main work room or clean room there should be ample refrigerting space to receive and cool all food needed. This refrigerator should be equipped with more coils than are usually installed in the standard refrigerator, for the reason the hot milk, after having been

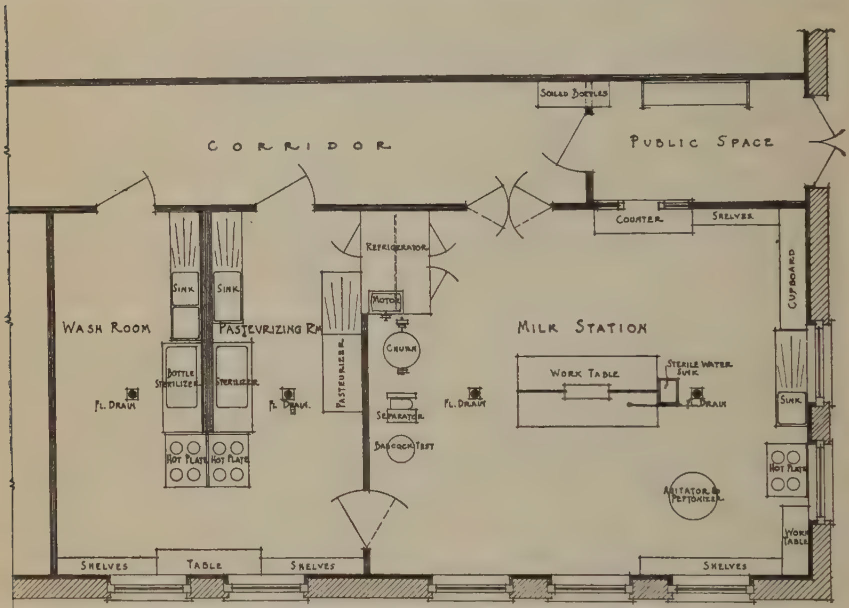


FIG. 265.—Plan of milk station, consisting of wash room, pasteurizing room, a work room and public space.

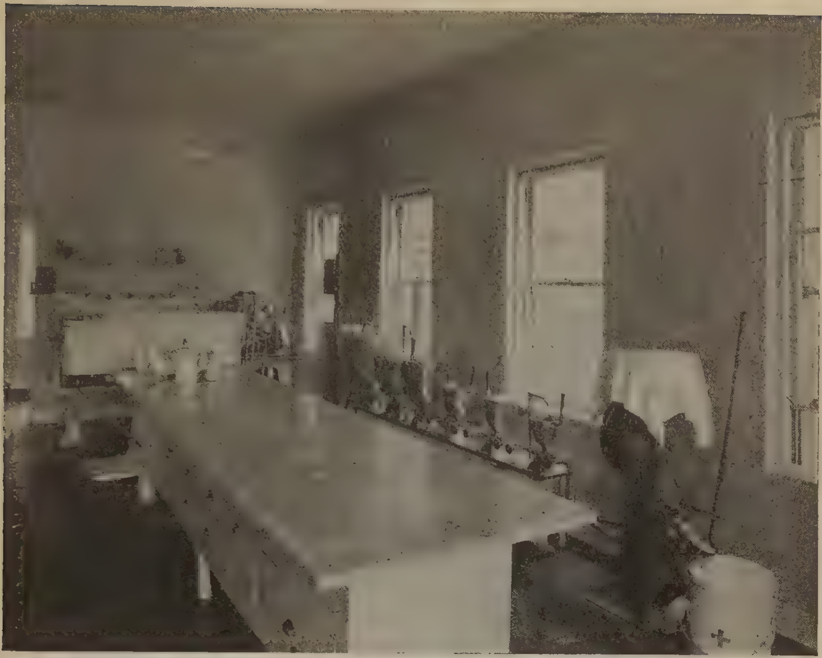


FIG. 266.—Milk laboratory. Babies Dispensary, Cleveland, Ohio. (Abraham Garfield, architect.)

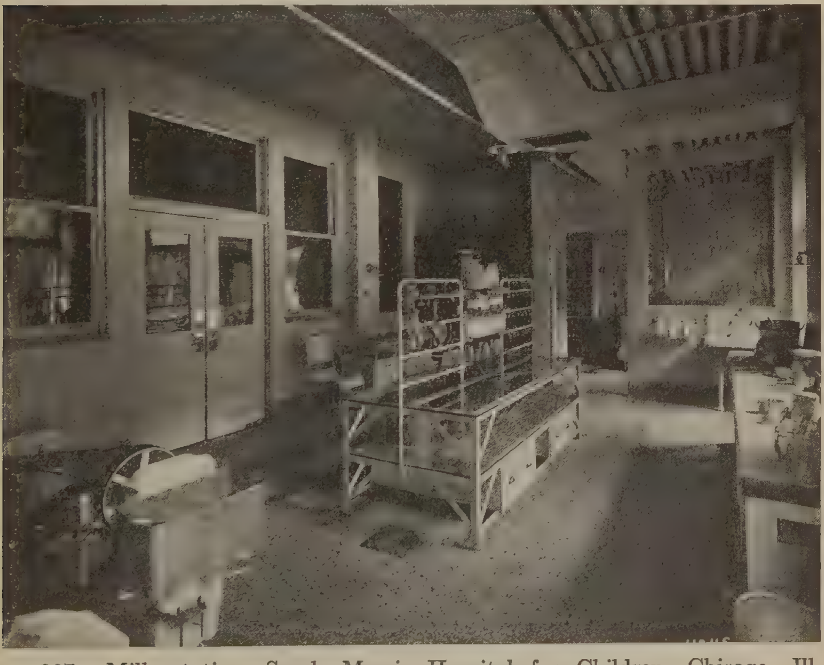


FIG. 267.—Milk station, Sarah Morris Hospital for Children, Chicago, Ill. (Richard E. Schmidt, Garden and Martin, architects.)

pasteurized, must be rapidly cooled by storing it in the refrigerator. Pasteurizing at best is only a partial sterilizing process and the refrigerator is very essential for preserving the food even after it is pasteurized.

In the work room, the milk can be best tested in a Babcock tester, so as to determine the amount of fat it contains, and is measured and put into the sterilizer, bottled ready for use. In many cases special foods are cooked and added to the milk portion of diet, and to accomplish this, it is necessary to have the room equipped with large work tables, a hot plate for preparing the special foods and for heating water for special uses. If possible, sterile water should be piped to this room.

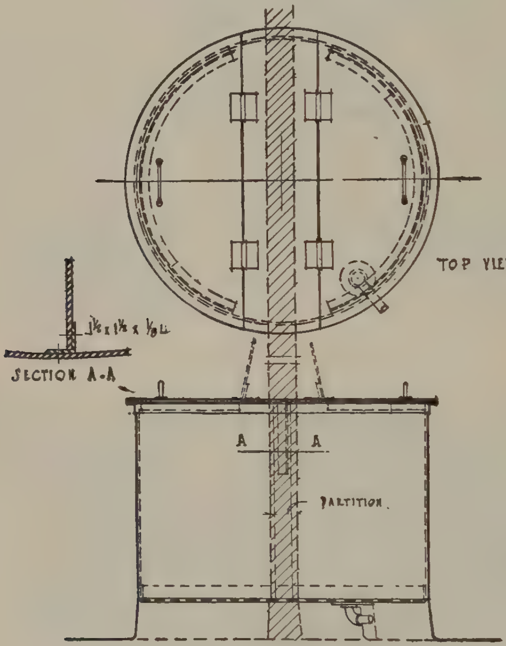


Fig. 268.—Sterilizing vat.

A separator to reduce the amount of fat in the milk is an important item. This can be of any standard make. A small churn should be provided, also a peptonizer, which in reality is a milk cooking and agitating machine, equipped with gas burners for heating the mixture. Several different combinations of foods can be cooked or heated by this machine at the same time. The usefulness of this machine is that it eliminates the otherwise necessary constant stirring during the cooking and mixing process. Metal shelves and counters should be provided in this department to store the supplies and the required utensils. It is quite important to have an accurate weighing scale and special attention should be given to the selection of all apparatus needed and used in this department. The tinning of all metal utensils should be perfect. Where milk is dispensed to the public there should be a conveniently located entrance, public space with a table for depositing used bottles, etc., and a counter or table over which the sterile supply is dispensed, without the likelihood of a re-use of a container until it has been sterilized again. The whole department must be kept spotlessly clean. Floor drains in the floor of each room and a good supply of hot water should be available for properly cleaning the floors and walls (Figs. 265–267).

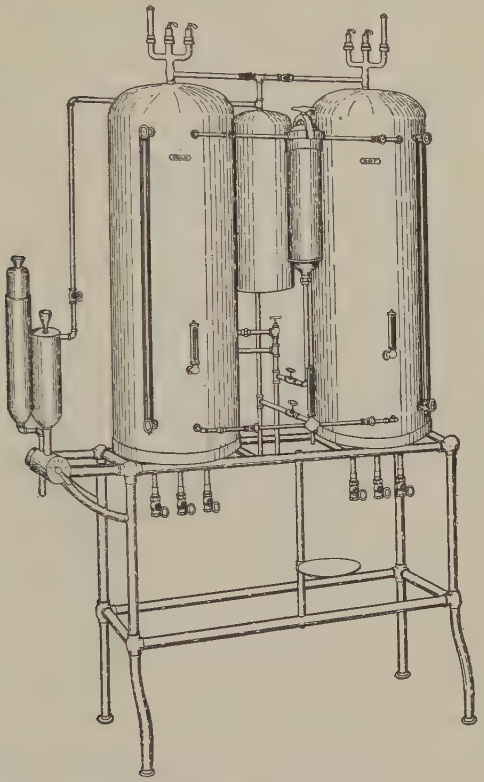


Fig. 269.—Saline solution apparatus. Consisting of filter, water sterilizer, measuring valve, hot and cold solution tanks, mixing chambers, interconnecting pipes, valves, etc. The interior surfaces of the still, storage tank, pipes and reservoir are lined with pure English block tin, heavily plated with silver so that the solution will not be in contact with any other substance.

Sterilizing Vat.—Inasmuch as it is not permissible to send all bedding, underwear, linen, etc., to the laundry together, some of the articles should be soaked in a disinfecting fluid and wrung out before sending to the laundry. For this purpose a vat built like the one illustrated in Fig. 268 is a convenience. The soiled articles can be deposited on the hospital side of a partition or wall and removed by the laundry help in a passage or outdoors without entering the hospital or isolation department. The wringer ought to be on a swinging bracket so that it can be moved out of the way to open and close the outer lid.

CHAPTER CXCII

MEDICO-LEGAL

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Medico-legal post-mortem examination of the body of a newly born infant is a somewhat more complicated operation than is such an examination of the body of an adult. For in addition to determining the cause of death it may be necessary to determine (*a*) whether the infant is newly born; (*b*) the maturity and viability of the child; (*c*) whether it was born alive or dead; and (*d*) how long it survived after birth. In order, therefore, to attain these objects it is essential to make certain special investigations of the body and to employ certain modifications of the general technic of necropsies.

Inspection of the external surface of the body should include a determination of its length and weight; the diameters of the head and shoulders; the condition of the skin, whether it is wrinkled or smooth, macerated or not, etc.; the presence and amount of lanugo; length of the finger and toe nails; location of the umbilicus with reference to the long axis of the body; the condition of the cartilages of the nose and ears; condition and size of the labia majora, especially whether they completely cover the labia minora; the location of the testicles; condition of the umbilical cord, especially whether it was cut or torn across, whether it was properly ligated and the presence of any hyperemia or other signs of inflammation in the skin about the insertion of the cord; length of the scalp hair; presence or absence of the pupillary membrane which disappears at the eighth month; size of the fontanelles; presence of smears of meconium on the body; signs of external injuries of any kind; presence or absence of foreign bodies in the mouth, nose and pharynx; and signs of post-mortem decomposition.

Examination of the Head.—After careful examination of the outer surface of the scalp for possible injuries, the usual incision is made from behind one ear over the top of the head to a similar position behind the other ear. The flaps of the scalp are reflected forward and backward, respectively, and their under surfaces examined carefully for edema (caput succedaneum) and hemorrhage. The external surface of the skull thus exposed is gone over thoroughly for the detection of any injury in the form of subperiosteal hemorrhages or fissures or actual fractures of the bones. The longitudinal sinus is next opened with scissors where it lies within the anterior fontanelle, the incision being continued along the sagittal suture to the lambda.

Because of the very firm adherence of the dura mater to the skull in infants the technique by exposing the brain is somewhat different from that employed in adult bodies. With heavy blunt pointed scissors incisions are made from the center of the anterior fontanelle downward along the frontal, coronal, sagittal and occipitoparietal sutures. At the lowest points of these incisions, horizontal cuts through the bones may be made for from 1 or 2 cm. The four bony flaps thus made may be opened out like the petals of a flower and the brain exposed. Note is made of the presence or absence of subdural blood clots and contusion of the brain substance. Technique of removing the brain is not different from that employed in adults. Because of the extreme softness of the brain substance of the newborn, it is difficult to remove this organ from the skull without injuring it.

The spinal cord can be exposed and examined by the usual incision along the midline of the back and then cutting through the transverse processes of the vertebræ with scissors. Or it may be removed after the body has been eviscerated by cutting away the bodies of the vertebræ with scissors.

To open the body an incision is made from the chin to a place about 2 or 3 cm. above the umbilicus. From this point an incision is carried downward on each side of the navel to the symphisis pubis, leaving the umbilicus at the apex of a narrow triangular flap of skin. Otherwise the opening of the body is similar to that employed in adults. The umbilical vein and arteries are now carefully examined by slitting them open with fine scissors. Incisions can be made transversely into the umbilicus from the peritoneal surface for the detection of pus or other evidence of inflammation.

It is necessary, before opening the chest, to determine the level of the diaphragm.

The examination of the viscera of the peritoneal cavity does not differ materially from that examination in adults, except in the following respect: Double ligatures should be placed on the cardiac end of the stomach; at the distal end of the duodenum; at the ileocecal valve; and on the rectum. Incisions are made between these ligatures in each instance, and the stomach, small intestine and large intestine, thus separated, are placed one at a time in a tall wide vessel of clean water to determine whether they float or sink. Sometimes it may be desirable to open the stomach under water to observe the escape of any air or gas that may be present.

After the trachea is ligated tightly in the neck, the **chest cavity** is opened in the usual manner by incision through the costal cartilages. The thymus is removed, weighed and measured. The trachea is cut across above the ligature and is removed with the thoracic viscera. The heart is examined for external evidence of possible malformations and the ductus arteriosus is explored by incising the pulmonary artery with scissors. Its opening is found on the upper wall of this vessel just proximal to its bifurcation. The degree of closure of this duct should be noted. The entire mass of thoracic viscera are now placed in a large vessel of water in order to test the buoyant power of the lungs.

The heart is now removed. The lungs and trachea are placed in a large deep vessel of clean water to determine whether they float or sink. Then each lung is removed by cutting through the corresponding bronchus and vessels at its hilus. The power to float of each lung is then tested. The separate lobes are then cut apart and each lobe placed in the water. If the lungs sink small pieces should be cut from various parts of the different lobes and placed in the water. If the whole lungs or any part of them float, small pieces should be squeezed very firmly between the thumb and finger and their power to float again tested. This is for the purpose of differentiating buoyancy due to normal aeration by respiration, from that which results from the presence of gas due to putrefaction.

The heart is now examined for evidence of malformation. The condition of the foramen ovale is to be carefully noted.

The examination of the liver, spleen and kidneys does not differ materially from that employed in necropsies on bodies of adults.

The subcutaneous tissues and muscles of the neck, especially the sternocleidomastoid muscles, are carefully examined for the presence of hemorrhage. The mouth, nasopharynx and larynx are explored for foreign bodies.

If desirable the inferior maxilla may be disarticulated and slices cut horizontal to its superior border in order to examine the centers of ossification. The sternum may also be cut through longitudinally in the median line for similar purpose. The center of ossification in the lower epiphysis of the femur is to be examined and its greatest diameter measured. This is spoken of as Beclard's center of ossification. In order to expose this center a U-shaped incision is made below the knee cap, the joint opened, and the cartilage of the epiphysis is cut into thin slices in a plane perpendicular to the long axis of the femur. It may be desirable to expose the lower end of the other femur and make an incision nearly parallel to the long axis of the bone and so as to include both bone and cartilage in order to expose the osteochondral junction. This is for the purpose of demonstrating syphilitic osteochondritis, should it be present.

Proof that an infant is newborn may be easy, if the placenta is still attached, or if the skin is still soiled with blood, meconium and vernix caseosa. Without these very definite evidences one must depend for an answer upon the presence of those characteristics of a full-term infant, to be described in detail later.

MATURITY OF THE FETUS

It is necessary in post-mortem examinations of the newborn to determine as accurately as possible the age or state of maturity of the fetus. To this end, the measurement of the length of the child is the most accurate means. For this purpose the crown-heel length, or standing height, and the crown-rump length, or sitting height, are taken. A somewhat less reliable element is the weight of the body. In the following table the estimated ages and lengths of human embryos are according to Mall, and their weights according to Fehling (Prentiss, C. W. and Arey, L. B., "A laboratory manual and textbook of embryology," Philadelphia (1917)):

Age	Crown-heel length (C.H.) or standing height in mm.	Crown-rump length (C.R.) or sitting height in mm.	Weight in grams
21 days	0.5	0.5	
28 days	2.5	2.5	
35 days	5.5	5.5	
42 days	11.0	11.0	
49 days	19.0	17.0	
2nd month	30.0	25.0	
3rd month	98.0	68.0	20
4th month	180.0	121.0	120
5th month	250.0	167.0	285
6th month	315.0	210.0	635
7th month	370.0	245.0	1220
8th month	425.0	284.0	1700
9th month	470.0	316.0	2240
10th month	500.0	345.0	3250

For practical purposes two rules may be used for determining the length of a fetus of a given age, and therefore, the age of á fetus of a given length. Up to the fifth month, the square of the number of the month gives the approximate length in centimeters of the fetus for that month. After the fifth month, 5 cm. are to be added to length at that period for each month after the fifth. For example: At the eighth month the length would be about (5 × 5 + 3 × 5 = 40 cm.). The approximate length after the fifth month can also be obtained by multiplying the number of the lunar month by five.

The child increases more rapidly in length and in weight while in the uterus than at any period of its life. As De Lee remarks "from the fifth week the fetus doubles its length five times, and its weight is 800 times greater at term than at two months." However, the length and weight vary in different individuals *in utero* just as in extra-uterine life. So that the figures in the table given above are only approximate.

Other characteristics also are useful in determining the age of a fetus. The intra-uterine life of the child is usually divided into two periods: The embryonic period, or first three months during which the organs are forming; and the fetal period, during which the completely formed organs increase in size. The characteristics of the child during the first three months can have little medico-legal importance. From the end of the third month the fetus shows the following features, according to the month of gestation.

At the end of the third month the body resembles that of a human being and measures 9 cm. in length. The head is proportionally very large and the neck is only a shallow groove. The umbilicus is closed. The ovaries and testes are differentiated, the external genitals are alike in both sexes. Centers of ossification are visible in several bones.

End of the Fourth Month.—All parts of the fetus are distinctly formed. The head is still relatively large. The skin is transparent, and reddish in color, especially over the face, palms and soles. The sex can be determined. The anus is open. The umbilical cord is inserted a little above the symphysis pubis. The arms are longer than the legs. The skeletal muscles are capable of movements. The duodenum contains meconium and bile. The liver is large.

End of the Fifth Month.—Length about 25 cm. The head is still relatively large and composes about one-fourth the length of the body. The fetus is lean, but the beginning deposit of fat causes the skin to lose its transparency. Lanugo is present all over the body. Finger and toenails are formed. The eyelids are closed. Centers of ossification are present in the astragalus and in the upper part of the sternum.

End of the Sixth Month.—The parts of the body have acquired more normal proportions. The fetus is still lean and the skin is wrinkled, although fat is somewhat more abundant. The skin is covered with vernix caseosa. Scalp hair, and eyebrows and lashes are present. The eyelids are open. The pupillary membrane is present. Meconium is in the small intestine. There is bile in the gall-bladder. The ovaries and testicles are below the kidneys.

End of the Seventh Month.—The skin is still wrinkled, but slightly less red. The scalp hair is several millimeters in length and is beginning to show color. The cecum has reached the right iliac fossa. The testicles are near the inguinal ring. Such an infant may survive after birth.

End of the Eighth Month.—The body is somewhat more rounded out. The skin is less red. The insertion of the umbilical cord is a little below the mid-point of the long axis of the body. The pupillary membrane has disappeared. The testicles are usually in the scrotum. Meconium is in the large intestine. A child born at this stage may be reared if given proper care.

End of the Ninth Month.—Length 46 to 48 cm. The skin is paler and the wrinkles have become smoothed out by the deposition of subcutaneous fat. Lanugo begins to disappear from the face and abdomen. The nails are at the tips of the fingers. The vital organs are fully developed and such a child may readily survive if given special care.

At Term.—The fully developed mature fetus measures about 50 to 51 cm. in length (34.5 cm. sitting height) and weighs from 3250 to 3400 gm. The length is a more reliable index of maturity than is the weight, but even this may vary within rather wide limits. Casper, in his series of measurements, reports a full-term fetus only 40 cm. long. Elsaesser made a similar observation and reports a maximum length of 65 cm. The weight shows still greater variations. A nine months' pregnancy may produce a child of only 1700 gm. (3½ lb.) while one of eight months may develop an infant of 3840 gm. (8 lb.) (De Lee). A maximum weight of 5500 gm. is reported by Merkel, 6500 gm. by Baudelocque, 7000 gm. by Neumann, and 9000 gm. by Cazeaux. These very exceptional weights may have been due to prolonged pregnancy.

Various factors influence the size acquired by infants *in utero*. Disease, especially prolonged febrile diseases, such as typhoid fever, and such chronic diseases as tuberculosis, diabetes mellitus, etc., in the mother produce small, weak infants. Women who work hard during the last month or so of pregnancy usually have smaller children than those who rest in a hospital during this time. The first child is usually smaller than later ones born to the same mother.

The skin and its appendages of an infant born at full term have certain fairly definite characteristics. The skin is white or pink in color, a fleshy red color denoting prematurity (De Lee). It is firm and elastic and beneath it is a layer of subcutaneous fat. A layer of sebaceous material (vernix caseosa) covers the skin and is especially abundant about the articular folds in the axillæ and over the cervical and lumbar regions. The lanugo has almost entirely disappeared, remnants of it being still visible over the shoulders. The scalp hair is colored and measures 2 to 3 cm. in length. The nails are firm and cornified and project slightly beyond the tips of the fingers, but only to the ends of the toes. The cartilages of the nose and ears are well formed and easily palpable.

The umbilical cord is inserted about 2 cm. below the center of the long axis of the body.

In male infants, the scrotum is red and wrinkled and contains the testicles, except in cases of cryptorchidism. In females the vulva is closed and the labia majora ordinarily completely hide the clitoris and the labia minora.

The diameters of the full-term fetal head vary within limits, partly because of differences in size of infants and partly due to molding of the head by the process of labor. The average diameters are as follows (De Lee):

Biparietal diameter	9.5 cm.
Bitemporal diameter	8.0 cm.
Suboccipitobregmatic diameter	9.5 cm.
Occipitofrontal diameter	11.0 cm.
Occipitomental diameter	13.0 cm.

The suboccipitobregmatic circumference measures 31 cm.; the occipitofrontal 34 cm.

The length of the foot may have some significance. A foot 8 cm. or more in length is probably that of a full-term fetus.

Measurements of the different bones can only be done after severe mutilation of the body, but they may yield information of value, especially in those cases in which the body has been dismembered and only parts of it are found.

In the following table, the measurements are averages from figures given by Merkel and by Casper:

Clavicle	3.9 cm.
Humerus	7.8 cm.
Radius	6.9 cm.
Ulna	7.2 cm.
Femur	9.0 cm.
Tibia	8.2 cm.
Fibula	8.0 cm.
Height of 7 cervical vertebræ	3.9 cm.
Height of 12 thoracic vertebræ	10.1 cm.
Height of 5 lumbar vertebræ	4.1 cm.

Centers of ossification in certain bones are of considerable importance in determining the maturity of a fetus because they can be found and measured in bodies that have undergone advanced decomposition. All four centers of ossification are present in the sternum; and that in the cuboid bone is demonstrable. The most important center for medico-legal purposes is that in the lower epiphysis of the femur. This was believed by Beclard, who first described its significance in this connection, to appear within the last two weeks of pregnancy. This small mass of bone in the midst of the epiphyseal cartilage is best demonstrated by making serial sections, 1 to 2 mm. thick, through the cartilage with a heavy scapula. In most instances Beclard's original idea of the significance of this center of ossification holds true. However, in rare cases it has been found absent in full-term infants. Thus Hecker was unable to demonstrate its presence in 15 out of 91 full-term infants; Liman in 14 of 413 cases; Hartman in 12 out of 102 cases. On the other hand, "Beclard's point" has been found as early as the eighth month by Hartmann in 2 out of 40 eighth month fetuses. The size of this center of ossification varies from 1 to 9 mm. in diameter, the average being about 5 mm. The variations in size do not, however, enable one to determine the age of a fetus or the length of survival of a newborn infant. In almost all cases, the size of the centers is equal in the two femurs. But occasionally inequalities have been observed and even its absence on one side has been recorded, as by Hecker in 3 out of 91 cases. The absence of this center of ossification does not, therefore, justify one in concluding, on this basis alone, that the fetus had not reached full term. Nor does its presence prove that full term has been reached. The expert would therefore be justified only in stating that an infant in which Beclard's point was present had either reached full term or had very nearly so. The importance of "Beclard's point" is rendered greater by the facts that it can be demonstrated and measured in infants the remainder of whose bodies have undergone more or less complete decomposition;

and that it can be utilized in cases in which only parts of the body are found, provided these include the femur.

At term, the lower jaw usually shows five septa which form four distinct tooth-sockets. This is considered by some as significant as the point of ossification in the lower epiphysis of the femur, in determining the maturity of a fetus.

Examination of the viscera yields little or nothing of value, in answering the question as to the maturity of a given fetus.

To answer this question one must consider the sum total of the characteristics described above. These characteristics may be grouped into principal and accessory, according to their significance. The accessory characteristics are those which concern the external appearance of the body, such as the condition of the skin, nails and hair; presence of lanugo; insertion of the umbilical cord, etc. The principal characteristics are those which really indicate the anatomical development of the fetus such as the length of body; diameters of the head; point of ossification in the lower epiphysis of the femur; and the condition of the inferior maxilla.

If all of the principal characteristics are present; e.g., if the fetus weighs at least 3250 gm.; if it measures at least 50 cm. in length; if the diameters of its head are as given above; if the center of ossification in the lower epiphysis of the femur measures at least 8.5 mm. in dameter; and if the lower jaw contains in each half five septa separating four alveoli; then one is justified in stating with some positiveness that the child was born at full term. If, however, the principal characteristics are barely within the minimum normal limits, one is justified only in stating that the given fetus had reached a stage of development that was approaching full term.

VIABILITY

By viability is meant the capability of a fetus for continued existence after removal from the uterus. This has little or no medicolegal significance and will be only very briefly discussed. Viability depends, first of all, upon a sufficient degree of development of the organs of the body to enable them to function in extra-uterine life. This condition is not reached until about the end of the seventh month. A fetus born at the end of the fifth month can only survive for a few minutes and make weak attempts at respiration. At the end of the sixth month, the infant can live for a few hours and breathe superficially. Even at the end of the seventh month, only the utmost care will enable the child to survive.

In the second place, viability depends upon a normal formation and normal relationship to each other of the different vital organs. Severe malformations are incompatible with life. Fortunately, monsters, such as cranioschisis, anencephalia, cyclopia, etc., do not survive. Infants with congenital hydrocephalus live only a short time. Severe malformations of the heart usually result in death of the infant very soon after birth. Congenital tracheo-esophageal fistula and atresia of the gastro-intestinal tract cause early death, unless successful surgical interference is possible.

Finally, viability is dependent upon the absence of any severe pathologic condition, developing *in utero*. The most important of such conditions is syphilis. This frequently causes death of the child before birth. But if it is born alive the pathologic changes in its lungs so interfere with their proper functioning that survival is for a short time only. Very rarely fetal peritonitis, or one of the acute infectious diseases from which the mother suffers, may cause the death of the infant, either *in utero* or very soon after birth.

Was the Child Alive during or after Birth? Tests of Life after Birth. Duration of Life after Birth.—In a medico-legal necropsy upon the body of a newborn infant, it is necessary to determine whether the child died (*a*) *in utero;* or (*b*) during the process of birth; or (*c*) after birth. It is essential, therefore, to describe in some detail the changes found in such a body that will enable one to decide the matter with some degree of definiteness.

Death of the Fetus in Utero before the Onset of Labor.—Death of the child in the uterus one or more days before the onset of labor has little medico-legal importance except in so far as the condition must be differentiated from death during labor or after birth. Intra-uterine death may occur at any stage in the development of the fetus; and the changes in the fetus vary somewhat according to the time at which death occurs. After the body of the child is well formed and developed, intra-uterine death results in maceration or, much more rarely, between the second and fifth months, in retention and mummification or partial calcification (lithopedion).

Maceration begins about the third day after death and is usually quite distinct after the fifth day. The condition ordinarily becomes more and more pronounced as time elapses. In the process of maceration, the skin takes up water, becomes reddish-brown in color, and the epithelium becomes easily detached or raised into bullæ. Later fluid is imbibed by the subcutaneous tissues so that the body becomes swollen and deformed. When laid upon the table, the body flattens out like a bag half filled with fluid. The head is swollen; the face is disfigured; and the skull bones are abnormally mobile. The various joints of the body are loose and are easily moved in abnormal directions. The epiphyses of the long bones may become detached. The serous cavities contain blood-tinged fluid. The viscera are softer than normal and are of a dirty-red to a coppery color. The umbilical cord is swollen.

It is not possible to determine with any great amount of definiteness from the degree of maceration of the fetus the length of time it has been dead. Occasionally maceration proceeds very rapidly; and on the other hand, one sometimes encounters a fetus known to have been dead for some days but with little evidence of maceration.

Death of Fetus during Labor.—Death of the child during labor is usually due to one of three conditions arising during the process of birth, namely: (1) Asphyxiation due to premature interruption of placental respiration; (2) injuries to the head; or (3) hemorrhage, placental or umbilical. The lesions observed in the bodies of infants dying during labor differ somewhat according to the cause of the death.

1. Asphyxia Due to Premature Interruption of Placental Respiration.—This results either from premature separation of the placenta or from compression of the umbilical cord. The latter may result either from prolapse of the cord with compression between the fetal head and the pelvis; or from coiling of the cord around the neck or limb of the child or, more rarely, from knotting, possibly also from torsion, of the cord.

The lesions found in the body of an infant thus asphyxiated are fairly characteristic. During intra-uterine life the child is in a condition of apnea. Its lungs are not aerated and contain relatively little blood. When, for any reason, placental respiration is interfered with, attempts at respiration occur. This leads to two characteristic conditions; it causes the aspiration of amniotic fluid and its contents into the trachea and bronchi; and the drawing of blood into the vessels of the lungs. Hence, one examines grossly and microscopically the contents of the trachea and bronchi for fluid, squamous epithelial cells from the skin (vernix caseosa), lanugo, meconium, mucus and blood. The depth to which these substances penetrate the bronchi depends upon the viscosity of the fluid and the force of the aspiration. Sometimes the material is found in the finest bronchioles and vernix caseosa and lanugo are even seen in the alveoli in microscopic sections.

Amniotic fluid and its various constituents may be swallowed and found in the stomach. The mere presence of normal amniotic fluid in the stomach has little significance. However, the presence of meconium in the swallowed fluid is of great importance; because meconium is not passed during normal intra-uterine life, but is very frequently expelled in intra-uterine asphyxiation.

It may be added that the presence of any congenital obstruction of the upper air passages or of the esophagus may prevent the aspiration or swallowing of amniotic fluid.

The lungs of the child during intra-uterine life are in a condition of fetal atelectasis. They are airless, will sink in water, are of a pale pink color and little blood escapes from the surfaces made by sectioning. The greater part of the blood from the right side of the fetal heart passes through the pulmonary artery and ductus arteriosus to the aorta, only a relatively small amount going through the lungs. Attempts at respiration, however, cause marked changes in intrathoracic pressure with the result that blood is drawn into the vessels of the lungs. These organs then assume a dark-red to purple color. From the surfaces made by sectioning relatively large quantities of blood escape, without any admixture of air. The lungs will sink in water.

Intra-uterine asphyxiation is further characterized by the occurrence of hemorrhages. These may appear in the form of small ecchymoses in the skin and mucous membranes such as the conjunctiva and inside of the mouth. Even more frequent and characteristic are the punctate hemorrhages into the serous membranes, especially in the pericardium and pleura. Small hemorrhages frequently are found also in the thymus and adrenals.

Hyperemia of the meninges is also commonly present. Ecchymoses may likewise occur here.

Finally, in cases of intra-uterine asphyxiation, the umbilical cord is usually bile stained. This is due to the evacuation during asphyxiation of meconium into the amniotic fluid.

The diagnosis of intra-uterine death from asphyxiations is, therefore, based upon (1) the presence of amniotic fluid with its vernix caseosa, lanugo and meconium in the air passages and stomach; (2) hyperemia of the lungs; and (3) punctate hemorrhages in the skin and the mucous and serous membranes. It is not always easy to determine the cause of the asphyxia. Grooves around the neck or limbs would indicate that coiling of the cord about these parts caused stopping of its circulation, and consequent asphyxiation.

2. Death Due to Injury of the Head.—Even in a normal birth the fetal head is subjected to great pressure, with some overriding of the cranial bones, with the formation of a caput succedaneum, and even with small ecchymoses in the scalp. In difficult labors, especially in those due to contracted pelves, the compression of the head is still greater. As a result of this, excessive overriding of the bones of the skull occurs, with tearing of blood-vessels and intracranial hemorrhages. Furthermore, the overriding and the flattening of the bones as a result of pressure, cause compression of the brain which is augmented by the hemorrhages itself. Compression of the brain may cause slowing of the fetal heart.

The more serious lesions produced by prolonged, difficult labors, and sometimes by precipitate labors, consist of intracranial hemorrhages and injuries to the cranial bones. The hemorrhage is due to laceration of blood-vessels by the excessive overriding of the cranial bones at the suture lines. The extravasation of blood usually takes place over one or both cerebral hemispheres; sometimes over the base; and still more rarely it may involve the substance and ventricles of the brain. Such a hemorrhage may be so great as to cause death before the birth is accomplished; or the child may survive for a few hours or one or more days; or it may recover entirely.

Injuries to the bones of the skull in difficult labors take two forms: Either there is a groove-like or cup-shaped depression of one of the cranial bones; or there is an actual solution of continuity with the presence of small fissures, or, very rarely, true fractures of the skull. Even these conditions are not necessarily incompatible with life.

Diagnosis of death, due to injuries of the head, are based, therefore, upon the absence of evidence of asphyxiation although these may also sometimes be present as a complication; and upon the finding of intracranial hemorrhage, and the lesions of the bones of the skull, described above.

3. Death Due to Hemorrhage.—Placenta previa; velamentous insertion of the cord; rupture of the cord, especially one that is abnormally short, are the more common causes of death of the fetus from hemorrhage.

Death of the Infant after Birth.—The proof of extra-uterine life elicited at post-mortem examination is based upon evidence that the infant breathed. For "to have breathed is to have lived." The establishment of respiration is manifested by three phenomena of prime importance; namely, (1) aëration of the lungs and (2) the filling of the pulmonary vessels with blood, which occurred at once and is therefore of immediate significance; and (3) the obliteration of the fetal circulation, which is slower in development and completion. The latter is of especial value in determining the duration of life after birth.

The special examination whose purpose is to determine whether the infant lived after birth begins, therefore, with a study of the lungs. To this end, their color, volume, consistency and ability to float in water are investigated. A true fetal lung is rarely seen because most cases of intra-uterine death are due to asphyxiation, and the lungs as usually seen at necropsy upon the newly born are hyperemic due to aspiration of blood in attempted respiration.

Fetal lungs are small, have sharp edges and occupy the back part of the small pleural cavities, being more or less covered by the heart and thymus. The aërated lungs of an infant are more voluminous, have rounded edges and completely fill the enlarged chest cavities and partially cover the heart. The volume of the lungs will vary with the completeness of aëration. The fetal lung is solid and somewhat liver-like in consistency; the aërated lung is softer, more elastic and is finely crepitant. The true fetal lung is uniformly pale in color, about the shade of uncooked breast of chicken. As usually seen at the post-mortem table, in cases of intra-uterine asphyxiation, the color is dark red to reddish-brown due to richness in blood. Respiration fills the lungs with air and blood, each having an effect on color directly opposite of the other. As a result, the color of the lungs of an infant who has breathed is mottled. The lighter, pink or rose, colored areas are those in which aëration is most complete while the darker red parts have less air and proportionately more blood. The less complete the aëration of the lungs, the more do they approach either the pale, fetal lung or the hyperemic lung of intra-uterine asphyxiation. The pleural surface of a well-aërated lung presents a fine mosaic design, best seen with a hand lens, and due to the fine net-work of blood-filled pulmonary vessels surrounding air-filled alveoli. This mosiac effect is absent in fetal lungs. Minute air vesicles can also be seen in the most fully aërated portions, and can be distinguished without great difficulty from the larger, more irregular subpleural bullæ that result from putrefaction. With weak respiratory efforts and only partial aëration of the lungs, areas of distinct mosaic tracery and air vesicles alternate with areas of darker red atelectasis in which these appearances are absent.

Surfaces made by sectioning the fetal lung are uniformly pale in color and quite anemic so that pressure causes only a few small drops of blood to appear. Similar surfaces of the lungs in intra-uterine asphyxiation are either uniformly dark-red in color or mottled light and dark-red, and pressure causes much blood to escape. The surfaces made by sectioning an aërated lung are mottled pale and darker red and blood mixed with fine bubbles of air escapes on pressure.

The ingress of air greatly reduces the density of the lungs. The unexpanded fetal lung has a specific gravity of about 1.045 to 1.056. It therefore sinks quickly in water. A lung completely filled with air is said to be about 770 times lighter than water. Even small amounts of air in the lungs quickly reduce their specific gravity to less than 1.000. So that the ability of the lungs to float in water is by far the most important test of extra-uterine life.

This test is performed as follows: Before opening the chest the trachea is ligated tightly just below the cricoid cartilage. The thoracic viscera are then removed along with the trachea which is cut off above the ligature. The whole mass is placed in a tall vessel of water. If the lungs have been completely aërated they will cause the entire mass to float. If the organs sink, the heart and thymus are removed and the lungs and trachea again placed in water. Before testing each lung separately for its ability to float the trachea and main bronchi are opened and their contents examined for amniotic fluid, vernix caseosa, etc. The lungs are then removed by cutting through the bronchus and vessels at its hilus and each lung is submitted to the hydrostatic test. If these still sink, the lobes are cut apart and each lobe is tested for its ability to float. Finally, if none of the larger divisions have floated, smaller pieces are cut from various parts of all lobes and dropped into water. If some of the pieces float, note should be made of the part of the lung from which they were taken. It is necessary, further, to press firmly between the thumb and finger some of the pieces which floated and replace them in water. It is not possible to so completely express inspired air from the lungs as to cause the pieces to sink in water.

As a rule this test is either very distinctly positive or equally definitely negative. Lungs which cause the whole mass of thoracic viscera to float are fully aërated. The degrees with which a whole lung or parts of varying size float furnish an index of the extent of aëration.

Although a positive hydrostatic test may be taken as evidence that respiration occurred, and, therefore, that extra-uterine life existed, there are certain possible sources of error that must be borne in mind. The lungs of a fetus born dead may be made to float as a result (*a*) of air introduced artificially in an effort to induce respiration; or (*b*) of gas, the product of putrefaction. Furthermore, the absence of air from the lungs at necropsy does not absolutely exclude the possibility of extra-uterine life nor even of respiration.

The insufflation of air into the lungs may be made through a tracheal canula or by mouth to mouth. In the latter case much of the air passes down the esophagus into the stomach. Lungs aërated in this manner show certain characteristics which enable one to differentiate them from lungs aërated by normal respiration. The insufflated air is not evenly distributed through the lungs. Hyperemia does not occur because there is no aspirating effect as in normal respiration. However, the insufflated lung of an infant dead from intra-uterine asphyxiation may be hyperemic. The absence of hyperemia causes the color to remain uniform so that no mottling is present. Finally, interstitial emphysema may occur if too much force is used in the insufflation. This can be demonstrated both grossly and microscopically.

The fact that gases originating from putrefactive changes may cause the lungs to float has a special medico-legal importance because frequently the bodies of newborn infants are not found until putrefaction is well advanced. The lungs of a newborn in a state of fetal atelectasis are singularly resistant to putrefactive changes and may be found in a fair state of preservation at a time when putrefaction is far advanced in other parts of the body. In fact, the researches of Bordas and Descoust indicate that the fetal lungs are more likely to undergo putrefaction without the production of gas. When gas is formed it is ordinarily only in moderate amount.

It is necessary, when the gas of putrefaction is found in the lungs, to determine whether the organs were primarily in a fetal (atelectatic), or in an aërated, condition. In the first place, the amount of gas in a putrefying lung is usually less in amount than the air in a normally aërated lung. Its distribution is less uniform than that of the air, and it is found chiefly in the form of small bullæ just under the pleura. A lung whose pleura is well studded with such bullæ and whose surfaces made by sectioning are riddled with numerous emphysematous cavities, is a lung which was originally aërated and not atelectatic. Small bits of lung containing putrefactive gas, after being pressed firmly between the thumb and finger, will sink in water. Such is not the case with a lung after respiration has been established, even when putrefaction supervenes. Finally, examination of the lungs with a hand lens, or sections of it with a microscope yields important information. In putrefaction, the gas is in the interstitial tissue of the lung; in a normally aërated lung the air is in the alveoli. In a lung with putrefaction only moderately advanced, areas of atelectatic lung tissue can be distinguished surrounding each bubble of gas. The uniform mosaic pattern seen on the pleural surface of a normally aërated lung is absent in one containing only gas of putrefaction.

It is possible also to obtain a negative lung test in bodies of infants who are known to have lived for a time after birth; and, on the other hand, to encounter a positive test in those known not to have breathed after birth. While these are exceptional cases, the possibility should be borne in mind, the sources of error understood, and expert opinion rendered cautious accordingly.

It occasionally happens that air is introduced into the cavity of the uterus during manual examination and in the application of forceps. Any attempts at respiration of the infant before birth could aspirate this air into its lungs. Although death might occur before the child was actually born, its lungs would show some degree of aëration, and the trachea and bronchi would also contain amniotic fluid, vernix caseosa, etc. The vigorous use of Schultze's method of resuscitation may cause sufficient air to enter the lungs to give a positive hydrostatic test. Such cases have little medico-legal importance because, in the first instance, there is no attempt to conceal the birth, and in the second place any person wishing to do away with an infant would hardly employ artificial means to establish respiration.

Failure to find air in the lungs in infants known to have lived after birth may be due either to the child's having survived for a short time without breathing, or the air may disappear from partially aërated lungs which return to their fetal condition. Premature and debilitated infants may be too weak to aërate their lungs. Subdural hemorrhage due to injury to the head during birth may lead to continuance of apnea and death from asphyxiation. Congenital obstructions in the air passages may prevent the establishment of respiration.

The absence of air from the lungs of infants known to have breathed may be the result of a gradual slowing down of respiration so that more air is expired than is inspired. This may lead to the freeing of the lungs of air by the time death actually occurs. Furthermore, the heart may continue to beat for some time after respiration ceases. Thus Hoffman reports a case in which the heart beat for two hours after the child stopped breathing; and Mattei has described a very remarkable instance in which the heart beat continued for 23 hours after respiration stopped. In such cases the air in the lungs becomes absorbed in the same manner as in an area of absorption atelectasis.

In view of the above possibilities, a prudent opinion in a case of an airless lung in a newborn infant, would be not that the child did not breathe nor live after birth, but that the lungs show no evidence that the child respired.

At the time of the establishment of respiration, air also enters the stomach. The mechanism by which this occurs is not altogether clear, but it is probably partly due to the aspirating effect of the descent of the diaphragm with the onset of respiration. Air is drawn into the esophagus as well as into the lungs. The distance to which it has penetrated in the intestines is an index of the duration of extra-uterine life.

To test the presence of *air in the gastro-intestinal tract,* double ligatures are placed on the cardiac end of the stomach, at the distal end of the duodenum, on the small intestine just proximal to the ileocecal valve, and on the rectum. The stomach and intestines are removed and the various parts are separated by cutting between the double ligatures. The stomach, small intestine and large intestine are separately placed in a wide and deep vessel of water and the ability of each to float is determined. A stomach well filled with air will float high in the water; one free from air sinks quickly to the bottom; while one partially filled will float half submerged in a vertical position. A small or large intestine well filled with air will float; one empty of air will sink; while the air-containing portions of one partially filled will remain at the surface with the empty parts submerged.

The absence of air from the gastro-intestinal tract is not proof that there was no extra-uterine life; nor does its presence prove that respiration did take place. The stomach and intestines may float because of the presence of gases due to putrefaction. This can usually be differentiated from an air-filled gastro-intestinal tract by the presence of bubbles of gas also in the walls of the stomach and intestine. Air may reach the stomach of a stillborn fetus by mouth to mouth insufflation; or as a result of intra-uterine inspiration of air introduced by manual examination or application of forceps.

With the rare exceptions noted above the presence of air in the stomach and intestines denotes the establishment of respiration. The results of the hydrostatic tests of the lungs of the gastro-intestinal tract, therefore, usually correspond. In a small percentage of instances the results are divergent. Thus in 449 collected cases, there were 39 in which the lungs were aërated and the stomach air-free. This is possibly due to a slower penetration of air into the stomach than into the lungs. In 271 collected cases there were 32 in which the lungs were atelectatic and the stomach contained air. There are three possible explanations of this condition: (1) Air entered both lungs and stomach, but the lungs later returned to a state of secondary fetal atelectasis by one of the possible means described above; or (2) the infant was too feeble to aërate its lungs. Neither of these explanations are wholly satisfactory. (3) The most likely cause is the aspiration of amniotic fluid into the lungs and air passages during intra-uterine partial asphyxiation. Attempts at respiration after birth are ineffectual because of the occlusion of the air passages and the air passes into the stomach.

Other tests of extra-uterine life that have been described, but are not now considered of much value, are: (1) Y-shape of cross-section of artery in umbilical cord; (2) "uric acid infarcts" in the kidneys. These latter have been found in infants known to have been stillborn. (3) Air in the middle ear was once considered a most important sign. At birth the middle ear is filled with fluid. Only gradually is this fluid replaced by air. Hence the presence of air in this cavity indicates not only that respiration was established but that it continued for some time.

The presence of foreign bodies in the air passages may furnish evidence of extra-uterine life. If the foreign material consists only of amniotic fluid and its contents, this signifies only that the infant attempted to breathe in a milieu containing this fluid. However, the presence of a wad of paper, cloth, etc., in the mouth and pharynx may generally be construed as indicative of extra-uterine life with commission of infanticide on the part of some one. However, even this must be interpreted only in the light of the other tests for extra-uterine life detailed above. Wounds of any kind (except those incident to birth) accompanied by hemorrhage are indicative of extra-uterine life.

Possible Duration of Extra-uterine Life.—Certain other tests not only furnish evidence of extra-uterine life, but give some idea of its duration. Microscopic examination of the stump of the umbilical cord may furnish important evidence. The presence of an inflammatory reaction indicates that life continued for at least 24 to 30 hours after birth. A distinct line of demarcation appears between the stump and the tissues of the abdominal wall in two to three days. The stump of the cord falls off in four to eight days and healing is complete about the eleventh day.

At birth meconium is present in both small and large intestine. Some of this may be expelled before birth if intra-uterine asphyxiation occurs. After birth the intestines empty themselves of this rather promptly. In very poorly fed babies, it may persist for as long as two to four days. The presence of food in the stomach is rare in cases of infanticide. The particles of vernix caseosa found normally in the stomachs of the newborn must not be mistaken for bits of food. The extent of the penetration of air into the gastro-intestinal tract is of great importance. If present only in the stomach there were probably only a few respirations. If air is found also in the small and large intestines, one is justified in concluding that life continued for several hours.

The extent of aëration of the lungs is of less value in determining the duration of extra-uterine life than is the distribution of air in the stomach and intestines. For the dilation of the lungs is a function of the vigor of respiration rather than of its duration. A vigorous infant will completely aërate its lungs in a few minutes.

The obliteration of the ducts and openings of the fetal circulation is not often of great importance from a medico-legal standpoint. The foramen ovale becomes closed within a few days. The ductus arteriosus collapses at the onset of respiration; its obliteration begins at its middle, extends toward the aorta and the pulmonary artery, and is not complete until about the third month of extra-uterine life. The ductus venosus Arantii is likewise rarely completely closed before the end of the third month.

To summarize: In estimating the length of survival after birth the two most important signs are the penetration of air into the gastro-intestinal tract and the condition of the stump of the umbilical cord. It is not possible to make such an estimation with mathematical exactness. If the lungs are well aërated and only the stomach contains air, death probably occurred very shortly after birth. If the lungs, stomach, and the large and small intestine contain air, the child probably survived for at least several hours. If the stump of the cord shows only the effects of drying without the establishment of a line of demarcation, death probably occurred within 48 hours. If the stump of the cord has dropped off, life continued for *at least* three days; and if there is complete healing at the site of the stump the child lived *at least* a week.

Occasionally it is necessary to determine approximately how long the child has been dead. The body of a newborn infant becomes cold quickly, *i.e.*, within five or six hours. The lips dry in a very short time. Post-mortem discoloration is evident in from three to six hours. Post-mortem rigidity may occur while the child is still *in utero.* It develops in about 45 minutes to one hour after death. It is to be remembered that because of the softness of the fetal tissues the rigidity is nothing like so marked as in an older person. It may also disappear rather quickly. Decomposition is much slower in its onset and progress in the newborn than in an adult.

INFANTICIDE

Infanticide, or the murder of a newly born child, is a crime of relatively great infrequency. The following table shows the number of homicides under one year as compared (1) with the total number of homicides in all ages, and (2) with the total number of deaths under one year in the Registration Area of the United States for a period of five years:

	1915	1916	1917	1918	1919
Homicides under 1 year.........	161	134	147	141	131
Homicides, all ages.............	4,670	5,050	5,754	5,456	6,836
Total deaths, under 1 year......	148,561	164,660	171,024	193,855	161,621

This table, of necessity (because of the manner of classification in the Mortality Reports of the Bureau of Census), includes the murders of newborn infants (infanticides) as well as those that are up to one year of age.

The following table shows the number of murders of infants as compared with the number of deaths under one year from the commoner causes per thousand births in the Birth Registration Area of the United States for the year 1919:

Deaths from premature birth..............	19.2	per 1000 births
Deaths from diarrhea and enteritis..........	15.7	per 1000 births
Deaths from congenital debility............	8.2	per 1000 births
Deaths from bronchopneumonia............	7.8	per 1000 births
Deaths from malformations................	6.3	per 1000 births
Deaths from injuries at birth...............	3.4	per 1000 births
Deaths from infanticide....................	0.07	per 1000 births

The means employed in committing infanticide are many and varied, but can very generally be grouped into (*a*) those in which great craftiness and cunning are used to avoid evidence of violence upon the body and (*b*) those in which extreme violence is employed. The first group includes by far the greater number of cases. The mortality statistics for infanticides for the Registration Area of the United States are not well classified. These cases are grouped under three divisions and the following table shows the number of murders of infants under one year due to each cause, over a period of five years:

	1915	1916	1917	1918	1919
Firearms	2	2	7	8	8
Piercing or cutting instruments	6	5	5	9	8
Other means	153	127	135	124	115

Haberda has analyzed the statistics of 211 necropsies in Vienna between 1896 and 1905, upon cases of presumed infanticide. Ninety-two cases of unquestioned infanticide were classified as follows:

Strangulation with a band or rope	9 cases
Strangulation with the hand	12 cases
Injuries of the throat	11 cases
Drowning in dirty water	22 cases
Drowning in amniotic fluid	12 cases
Drowning in cesspool	3 cases
Drowning in river	1 case
Burying alive in cinders	1 case
Burying alive in earth	1 case
Crushing	1 case
Fractures of the skull by direct blows	5 cases
Fractures of the skull by fall (without submersion)	2 cases
Accidents following submersion and injuries to the head	12 cases

In most of these infanticides other means were employed in addition to that under which the case is grouped.

Criminally induced deaths of infants may further be grouped as (*a*) crimes of violence and (*b*) crimes of willful and intentional neglect of the care which is essential to establish and maintain the extra-uterine life of the child. The crime of violence may be committed during the process of birth or after the child has been expelled from the birth passages. The former is exceedingly rare. Thoinot collected only three authentic cases from the literature. And yet under English law, if an infant's life is destroyed before it is *fully* born, the charge of murder cannot be made.

Of the infanticides due to violence, the vast majority are the result of some form of suffocation or "mechanical asphyxiation." Of these there are two groups: (1) Those due to *obstruction of the air passages* by some external object, as (*a*) constriction of the neck with a rope, cord or strap, or by the hand; (*b*) by obstruction of the nose and mouth by the hand or some other object placed over them; (*c*) or by obstruction to the movements of the chest. (2) In the second group are those cases in which the suffocation is due to some *foreign body or substance within the air passages themselves;* as (*a*) in drowning; or (*b*) burial alive in sand, cinders, etc.; or (*c*) by some object, a handkerchief, for example, forcibly pushed into the pharynx or larynx.

The newborn infant needs less oxygen than an older child or adult and shows a relatively greater resistance to being deprived of it. At least 10 minutes are necessary to cause death by the usual method of suffocation. Cases are on record of remarkably long survival after attempts at suffocation. Thus Bardinet describes an infant that was buried 25 cm. under ground and yet showed signs of life at the end of eight hours.

All of the above mentioned methods of suffocation have certain post-mortem signs in common. These will be discussed in some detail first and the distinguishing or diagnostic features of each method will then be described.

The most characteristic post-mortem sign of suffocation (or asphyxiation) from any cause is the presence of *petechial or ecchymotic hemorrhages into the serous membranes* and into the substance of different organs. These are usually more numerous in infants than in adults and constitute a most important finding. They are found in approximately 100 per cent. of infants dead from asphyxiation *in utero;* and in almost the same proportion of the newborn who have succumbed to suffocation. Of adults dead from suffocation from 15 to 25 per cent. show these lesions. The delicacy of the tissues and the fragility of the blood-vessels account for their relatively greater frequency in infancy.

The sites of predilection of these hemorrhages are the visceral pericardium and pleura and the surface of the thymus. Less commonly they are present in the peritoneum and the meninges. Not infrequently they are seen in the mucous membranes of the mouth and gastro-intestinal tract, in the conjunctiva and even under the skin.

These hemorrhages appear as small round or oval, dark-red spots or splotches from less than 1 mm. to several millimeters in diameter, just beneath the serous covering of the viscus. Their numbers vary greatly in different cases. In the pericardium they are more commonly found upon or near the origin of the great vessels, and range, ordinarily, from one to a dozen in number. The author has seen a hundred or more scattered over the surface of the heart, being most numerous on the pericardium-covered portion of the aorta, along the auriculo-ventricular groove and on the posterior surface of the heart along the interventricular groove. They are usually less numerous, or at least appear more widely scattered, in the pleura than in the pericardium. They are most commonly found near the hilus, especially on its posterior surface, and along the lower border of the lungs.

Two theories have been advanced to account for the occurrence of the subserous hemorrhages. The older theory, that they are due to the strong negative intrathoracic pressure resulting from vigorous attempts at inspiration, is not generally accepted. It is more likely that the increased arterial pressure which accompanies asphyxiation is responsible for their occurrence.

In older children, and in adults, subpleural and subpericardial punctate hemorrhages may be due to causes other than asphyxiation, as, for example, septicemia, purpura hemorrhagica, etc. Hence. in older persons these lesions do not possess the very great medico-legal importance assigned to them by Tardieu, who first emphasized their significance in this connection. But these other etiologic factors hardly pertain to the newborn. Hence subpleural and subpericardial hemorrhages in the newborn are almost pathognomonic of death from asphyxiation. In this instance, therefore, the other post-mortem indications of death from asphyxiation are not considered so much in the light of a support of the diagnosis of death from this cause, as means of determining whether the asphyxiation occurred *in utero* or after birth. If the death occurred *in utero*, the lungs and stomach will be free of air, and the trachea and bronchi will contain amniotic fluid with vernix caseosa, lanugo, and, possibly, meconium. If the asphyxiation occurred after the establishment of extra-uterine respiration, the lungs and stomach will be aërated and signs of violence or the presence of foreign substances in the air passages may furnish a clew as to the manner in which the asphyxiation was brought about.

The various methods by which infants are suffocated may now be considered. These are (1) strangulation (*a*) with a cord or strap, or (*b*) with the hand; (2) occlusion of the upper respiratory passages; (3) compression of the chest; (4) burial alive; (5) drowning.

Strangulation with a cord or band of some sort is one of the commoner methods employed in infanticides. A child murdered in this manner shows at autopsy aëration of lungs and gastro-intestinal tract; punctate hemorrhages in the pericardium; the imprint of the cord or band upon the neck, and local injury to the soft parts of the neck. The mark of the cord usually has the following characteristics: It extends horizontally completely around the neck, usually at about the level of the larynx, in a single, sometimes double groove, of fairly uniform depth; the skin is slightly abraded and is only rarely rendered hard and parchment-like. Such a lesion must be distinguished from natural, artificial and pathologic folds of the neck. In infants with a considerable amount of subcutaneous fat, bending the head forward causes the formation of a groove on its anterior surface that may be very distinct in a cadaver in cold weather. In such a case the epidermis in the groove is intact, the groove more or less completely disappears when the position of the head is changed and reappears when the head is brought back to its original position. Artificial grooves may be made after death by clothing. The imprint on the neck, in such cases, is soft and pale; not desiccated; the skin is intact; and the configuration of the mark is that of the object which made it. Irritation of the skin of the neck, as in intertrigo, may cause a circular band of redness or even of excoriation of the skin. This latter applies only to children two or more days old.

In the soft tissues of the neck of an infant dead from strangulation there are hemorrhages, but very rarely any severe laceration of the blood-vessels, and almost never any fracture of the thyroid cartilage or cervical vertebræ.

Sometimes the umbilical cord itself is used to induce strangulation because it will not produce the suspicious superficial injuries to the skin that a harder rope or band would produce. The claim is then made of death due to coiling of the umbilical cord about the neck *in utero.* The truth or falsity of this claim can be determined by measuring the length of the cord, by examining the grooving of the neck and by the condition of the lungs and stomach. Intra-uterine asphyxiation due to coiling of the cord about the neck is impossible in the case of short cords, or even with those of normal length. The cord itself must be abnormally long. There is usually more than one groove around the neck and a groove can usually be made out extending downward over one or other clavicle toward the umbilicus. The navel itself frequently shows distinct evidence of traction upon the cord. Finally, asphyxiation by coiling of the cord about the neck occurs *in utero* as a result of interference with placental respiration. The lungs and stomach will, therefore, not be aërated. If these organs contain air it is proof that the strangulation did not occur until after the establishment of extra-uterine respiration.

Suffocation may be induced by the use of the hand either by pressure upon the neck (choking) or by occluding the nose and mouth. The local lesions produced in choking are external and internal. On each side of the neck the skin shows scratches and crescentic impressions of the finger nails. These are usually more numerous on one side than on the other, right or left according to which hand is used. These injuries are more regular in distribution and usually less severe in an infant than in an adult because of the difference in the amount of resistance which the victim offers. Owing to the greater difference between the size of the hand and the child's neck, the marks of injury will extend further back and may even involve the entire circumference of the neck.

The face is usually hyperemic; the lips somewhat swollen and there may be petechial hemorrhages in the skin of the face, in the conjunctiva and in the mucous membranes of the mouth.

The injuries to the deeper tissues consist of hemorrhages into the muscles of the neck; less commonly, fracture of the larynx; and, still more rarely, fracture of the trachea and rupture of the large blood-vessels. The hemorrhage may be relatively large and the blood may suffuse the tissues all about the larynx. The muscles along the cervical spine and the thyroid gland may also show hemorrhages. This lesion must not be confused with the hemorrhage that occasionally occurs in the sternocleidomastoid muscle during birth. This results from a marked torsion of the head and neck, is almost always unilateral, rarely larger than 1 or 2 cm. in diameter, and is usually found near the center of the muscle. These injuries to the neck must also not be confused with those sometimes made by the mother when she attempts to help in the delivering of the child when she is alone at the time of labor. The distinguishing features of such injuries will be described a few paragraphs below.

The most common method of infanticide is suffocation by occluding the mouth and nose. This is most frequently accomplished either by turning the baby on its face in a soft pillow or covering the face with a soft cushion or cloth. Okamoto describes a case in which wet tissue paper was plastered over the infant's mouth and nose. In instances of this kind in which there are no superficial or deep injuries, there is no means by which such a criminal death can be differentiated from accidental death from suffocation of a baby under the covers in its bed.

Suffocation by closing the mouth and nose with the hand is a moderately common method of infant murder. Local injuries in the shape of deformity and flattening of the nose and lips, abrasions and marks of fingernails on the nose, lips and cheeks are of assistance in differential diagnosis.

The local injuries made by the hands in infanticide by suffocation may be confused with those induced by the mother, when she attempts to hasten by manipulation the delivery of her infant in clandestine births. The injuries produced by the latter means consist of injuries to the face and neck (or breach, in breach deliveries) and to the inside of the mouth. The differential diagnosis is based upon the localization and direction of the traumata. In criminal attempts, as in strangulation, the lesions induced are usually quite definitely limited either to the region of the mouth and nose or to the throat. Those which are the result of attempts at self-help on the part of the mother in labor are more widely and irregularly distributed. These differences are obviously due to differences in the objects to be attained. It has been asserted that the concave side of the crescentic marks of fingernails open upward in the lesions due to self help and toward the medium line or downward in cases of criminal attempts at suffocation; and further, that the scratches which frequently begin in a nail print are directed upward in the former and downward in the latter. However, these distinctions are finely drawn and in actual practice they often are very difficult to make.

Occasionally in attempts at self assistance in clandestine labor, the mother may place her thumb or finger in the child's mouth and cause a considerable degree of laceration of the tissues of the soft palate and pharynx.

Suffocation of the infant may be induced by the introduction of foreign bodies into the pharynx and larynx. Various substances such as hay, straw, wet paper, rags and even a stone have been used.

The proof of this method of infanticide is based upon the local injuries the presence of all or part of the foreign body in the mouth and throat and the internal evidences of death by suffocation. The local injuries vary in severity and consist of lacerations of the lips, tongue, palate and pharynx.

Suffocation by compression of the infant's chest is a not uncommon cause of accidental death in the newborn, the mother accidentally rolling over on the child while asleep. A similar method may be employed intentionally in a criminal manner. In all instances there are the internal evidences of death by asphyxiation and local injuries. These latter consist of contusions of the chest wall and sometimes of fracture of one or more ribs.

The crime of infanticide is sometimes accomplished by *burial* of the infant *alive* either in the ground, or in sand, cinders, sawdust, or any such substance. The process is equivalent to submersion in a solid medium. Death results from suffocation due partly to pressure on the chest but chiefly to blocking the air passages by aspiration of the material in which the body (or head) is submerged. The diagnosis of this method is based upon the finding of the general evidences of death by suffocation (subpericardial hemorrhages, fluid or partially clotted blood, etc.) in an infant whose lungs and stomach show aëration, together with particles of the submerging material in the mouth, nose, air passages, esophagus and stomach. Earth, sand, sawdust, etc., may enter the upper air passages of bodies placed in them after death. But the penetration is rarely further than the anterior part of the nose and mouth; occasionally as far as the larynx; and only very rarely into the trachea. It appears probable that such materials can only enter the stomach by the act of swallowing. Their presence in this viscus may be accepted as very definite evidence that the individual was alive when he became submerged in the substance in question. The presence of the material adhering to the skin or entangled in the hair is also important confirmatory evidence. Attention has already been called to the fact that the newborn may survive for remarkably long periods after being buried alive.

Drowning as a means of infanticide is not uncommon. The infant may be placed in a large vessel filled with water such as a bath tub, or may be thrown into a stream or lake, into a sewer, or into a cesspool. The medico-legal post-mortem examination of the body of a child found in such a place must determine (1) whether death was due to drowning, and (2) as far as possible, whether its presence in the water was due to accident or criminality. For this three possibilities exist: (*a*) That the infant was dead when placed in the water; (*b*) that its presence was due to an accident of precipitate labor; or (*c*) that the child was thrown into the water in order to destroy it.

The diagnosis of death by drowning in an infant is based upon much the same post-mortem signs as in an adult. The skin is cold; "goose-flesh" is present but not so evident as in an adult; the skin of the palms and soles is whitened and shrivelled. In the trachea, if the child has not been dead too long, there is a fine froth; water is present in the trachea, bronchi, lungs and stomach; the apices and anterior borders of the lungs are emphysematous; and, usually, there are petechial hemorrhages in the pericardium and pleura. A microscopic examination of the water in the lungs and stomach will reveal solid particles, e.g., sand, fecal matter, etc., which correspond to the materials in suspension in the water from which the body was taken. The finding of water and the substances suspended in it, in the lungs is not of as great significance as their presence in the stomach. For water can penetrate the lungs, even to some depth, after death. Its presence in quantity in the stomach, however, is the result of the act of swallowing, and, therefore, evidence that life still existed when the body entered the water.

Any injuries found upon the body may be the result of violence applied before the infant was thrown into the water; or they may be the result of striking the sides or bottom of the stream, etc.; or they may have been acquired in the convulsions of the death agony or as a result of being carried by currrents or waves against solid objects in the water.

All of the above applies to those cases in which death is the result of asphyxia. In other instances death results from "submersion inhibition." When the body enters the water in such a case, there is no struggle of any kind, no attempts at respiration, no swallowing of water. Hence, all of the common signs of death by drowning are absent. This type of death is not uncommon in adults, but appears to be less common in infants.

An infant not stillborn that accidentally falls into water as an accident of precipitate labor will show water but no air in its lungs and stomach. If the child was dead when placed in the water, the liquid may penetrate the upper air passages but not the stomach. Other pathologic conditions found in the body may indicate the cause of death. Without the presence of water in the deeper part of the lungs and in the stomach, the finding of subpericardial and subpleural punctate hemorrhages would indicate that death from asphyxiation preceded the entrance of the body into the water.

The death of an infant may result from **asphyxiation by gas.** This may be accidental or criminal. The author investigated such a case in which the mother was strangled to death in the room in which her baby was sleeping. The criminal, in an attempt to hide his crime and apparently without thinking of the infant, turned on the gas in the room and left the house. The mother showed evidences of death by strangulation; her heart's blood was very dark and did not clot well, and was free from carbon monoxide. The infant's right heart's blood was of a bright red color, not coagulated and contained a large amount of carbon monoxide. In the Coroner's Office of Cook County, Illinois, there are records of very many cases in which the mother committed suicide and infanticide at the same time by turning on the gas.

Fractures of the skull furnish the majority of the cases of infanticide by external violence. These may be produced by direct application of force, as, for example, a blow with a club; holding the child by its feet and striking its head forcibly against a table, wall, floor or other object; crushing the head under the foot of the murderer, etc. The results of such injury are (*a*) contusion or even laceration of the scalp, at the site of the blow; (*b*) fracture of the skull; (*c*) subdural hemorrhage; and (*d*) contusion of the brain. The extent and location of the fracture of the skull will vary with the method of application. If the body is hurled head first against a wall, the fracture may be on one side of the skull only. If the head is crushed between a heavy foot and the floor, there are fractures in both parietal bones. The size of the fractures varies from one or more fine fissures following the radiating lines of ossification, to a crushing of the bones into several, up to 20 or more, fragments. The subdural hemorrhage and contusion of the brain vary and may be very extensive. Hemorrhage into the lateral ventricles may even be thus produced.

2. The body of the infant may be allowed to fall head-foremost from a height. It has already been pointed out that the experiments of Chaussier showed that dropping a stillborn infant on its head from a distance of 18 in. resulted in fractures of the skull in 80 per cent. of cases. Allowing them to fall in a similar manner from a height of 1 meter or more caused very extensive fractures and even crushing of the skull with the production of much deformity of the head. It is only when great violence is used that the continuity of the scalp is broken and external hemorrhage and loss of brain substance occurs. This is probably due to the relatively greater softness and lack of rigidity of the infant's skull as compared with that of the adult.

It is often desirable to determine whether the fractures of the skull in a given case are the result of violence directly applied or the effect of a fall upon the head. This distinction is often difficult to make because comminuted fractures may be produced by either method. The injuries that are the result of a fall upon the head are usually not accompanied by other injuries elsewhere upon the body. Where the violence is directly applied, as with a club, there are frequently contusions on the face or shoulders. The phenomenon of injury to the brain by the effect of *contre coup* is not so frequent in children as in adults.

It is even more necessary to distinguish between fractures due to criminal violence from those due to accidental means, such as fractures occurring during difficult labor; those incident to precipitate labor; and those made after death.

The fractures of the skull resulting from difficult labor are small and usually merely tiny fissures in the bone that follow the radiating lines of ossification. These are almost always limited to one parietal bone. They therefore differ from the much more extensive comminuted fractures due to criminal violence. Furthermore, the excessive compression of the head which causes the slight fracture of the skull in difficult labor also usually results in the death of the fetus before extra-uterine respiration is established. In such a case, therefore, the lungs are in a condition of the fetal atelectasis and the stomach free from air.

Fractures of the skull resulting from accidents accompanying precipitate labor may be severe and extensive, or slight and insignificant according to the distance from which the child fell. This injury may result in death before the establishment of extra-uterine respiration and the lungs and stomach will be found airless. If, in addition to the fracture of the skull, the child drops into water, the lungs and stomach may contain water but no air if the child attempts to breathe. Signs of rupture of the cord should furnish confirmatory evidence of precipitate labor.

Post-mortem fractures of the skull often follow attempts to get rid of the dead bodies of infants, especially if illegitimate. These may be quite extensive. There may even be some hemorrhage about the site of fracture, but this is always relatively insignificant when compared with the bleeding induced by a comminuted fracture made *ante-mortem.*

The occasional defects in the skull bones and tardy or irregular ossification should not cause confusion in the diagnosis of fractures of the skull if such lesions are examined carefully and if it is remembered that these congenital defects are not accompanied by hemorrhage. In an infant with congenital hydrocephalus recently seen by the author at autopsy, there were very many, some quite extensive, defects in all of the bones of the vault of the skull.

Wounds of the membrane produced with *piercing or cutting instruments* are usually made with scissors or needles. Craft is frequently employed to render detection more difficult. The scissors may be inserted in the mouth and the vessels of the throat cut in much the same way as fowls are killed for market. Less commonly the scissors may be used for a stabbing instrument or be driven into the brain through one of the fontanelles or sutures. A needle may be inserted into the brain through the anterior fontanelle. The insignificant wound may be easily overlooked if the external examination is not very painstaking. The internal injuries are more evident, once the head is opened. Such an injury may result fatally in three different ways. (1) If the needle passes through or lacerates the superior longitudinal sinus fatal subdural hemorrhage may occur. (2) The movement of the needle about the wound in the skin as a fulcrum may so lacerate the brain as to quickly cause death. (3) Infection of the meninges may follow, and death result, after some days, from acute suppurative meningitis. Occasionally, a needle is inserted into the heart and by manipulation causes laceration and fatal intrapericardial hemorrhage.

The use of cutting instruments, such as knives or razors, is not a common method of infanticide. Occasionally the throat is cut. Still more rarely one or more limbs may be amputated. This latter must not be mistaken for an amputation made post-mortem or for a congenital amputation.

Very rarely infanticide is induced by poisoning. The post-mortem findings will vary with the substance employed. A chemical examination of the viscera may be necessary for the identification of the drug used.

Numerous dangers menace the newborn infant. If these are not guarded against, death results. If the mother is alone, as often happens in clandestine births, she may faint and remain unconscious for some time, or she may be too exhausted by the labor to be able to furnish the necessary care. Or, the mother or some other person may willfully and intentionally withhold the required attention to the needs of the child. It is very difficult to prove criminality in cases of death due to neglect, because the neglect may be due to lack of intelligence, or of physical ability. This latter applies especially to clandestine births. Conditions which may result in the infant's death are (1) occlusion of the air passages by mucus which must be removed to permit the establishment of extra-uterine respiration; (2) as the child lies between the mother's thighs its face may be covered with a part of the membranes, or be pressed down upon the surface of the bed, or be submerged in the mass of amniotic fluid and blood collected there; or (3) very rarely the child may be born within intact membranes. The cutting of the umbilical cord and protection of the infant against cold are two essential procedures to preservation of the life of the child. Failure to cut the cord is perhaps not fraught with irrevocable dangers to the child, but this failure is rather an indication of lack of care in general.

Exposure to cold is a very serious danger to the newborn. In proportion to body-weight and volume, the body surface of an infant is much greater than that of an adult. Radiation of heat is therefore relatively very rapid from the newborn. For this reason, exposure of abandoned infants on door-steps or on the street frequently results in their death even in only moderately cold weather. There are no characteristic findings at post-mortem examination.

Occasionally death of infants results from starvation. This may be due to some congenital malformation, such as esophageotracheal fistula, or congenital stenosis of the pylorus, or to criminal neglect.

SUDDEN DEATH IN CHILDREN

In another place we have discussed those causes of death in the newly born that are etiologically related either to intra-uterine development or to the events and accidents incident to the process of birth. It is now necessary to consider the commoner causes of sudden death in children after the first 10 days or two weeks of life succeeding birth. These are (1) acute bronchitis and bronchopneumonia; (2) enteritis and diarrhea; (3) "thymic-death;" (4) asphyxia from various causes; (5) marasmus; (6) internal hemorrhages; (7) acute peritonitis; (8) cardiac affections following acute infectious diseases; (9) lesions of the brain; (10) laryngospasm; (11) hemorrhage into the parathyroid glands; (12) deaths associated with eczema.

It is necessary to consider these more or less natural causes in some detail because (1) children are not infrequently found dead in bed or elsewhere without any previous indications of illness; (2) they may die with symptoms so alarming, of such sudden development and such short duration as to raise a question of possible poisoning, especially if there are any accompanying suspicious circumstances.

It must be remembered that the common causes of death in adults, e.g., pulmonary embolism, obstruction of a coronary artery, cerebral hemorrhage, etc., are almost never responsible for sudden deaths in children. Furthermore, some diseases that are usually either unimportant or at least not alarming in adults, e.g., bronchopneumonia and enteritis and diarrhea, may cause sudden death in children.

The most common cause of sudden death in children under one year of age is *bronchopneumonia*. Of 261 cases of bronchopneumonia in children under four years old, collected by Holt, 169 occurred during the first year and 73 during the second year. It may, as already mentioned, affect the newly born as a result of the aspiration of infectious material from the birth passages. It is not so common after the second year.

Sudden death from this cause is frequently not preceded by symptoms, or the premonitory symptoms are so mild as to be overlooked or misinterpreted. Very small and very weak children do not cough and may not show a rise in temperature. Or it may take place soon after the child has taken food or drink and thus arouse suspicion of poisoning. Not infrequently the child is found dead in bed.

The greater frequency of bronchopneumonia, as contrasted with the morbidity of lobar pneumonia, in young children is due largely to anatomical differences between the infant and the adult lung. In the lungs of infants the bronchi are more prominent and more numerous, compared with the bulk of the lung, and the air vesicles are smaller and not so well developed.

The appearance of the lung as observed at the post-mortem table, varies somewhat with the stage and type of the bronchopneumonia. The characteristic feature of all stages and forms is the presence of areas of consolidation scattered through one or both lungs with air containing tissue between. Seen through the pleura, these areas of consolidation are usually somewhat elevated and either dark-red or grayish in color. The surfaces made by sectioning such a lung are mottled dark grayish-red and light grayish or yellowish-red. In the midst of each area of consolidation a severed small bronchus or bronchiole is frequently visible. Pressure usually causes a purulent exudate to escape from the cut bronchi and bronchioles. Not infrequently there are seen depressed places on the surface of the lung of a very dark-red or purplish color and over which the pleura is finely wrinkled. These are areas of absorption atelectasis that result from plugging of the regional bronchus with exudate. Microscopically, the alveoli in the consolidated areas contain an exudate made up of a moderate number of pus cells and many desquamated epithelial cells with little or no fibrin. The bronchi and bronchioles contain a similar exudate. In very severe cases, such as one seen by the author, many of the bronchioles are completely denuded of their lining epithelium. The latter, together with pus cells, forms plugs which effectively occlude the bronchus or bronchiole, thus leading to the absorption atelectasis mentioned above. Ecchymoses are usually present in the visceral pericardium and pleura.

The cause of death in bronchopneumonia is partly the absorption of toxic substances from the focus of infection and partly, perhaps chiefly, asphyxiation. The latter is due not only to the filling of many alveoli with exudate but also to the fact that congestion in a large part of an affected lobe greatly reduces the air-containing space because of the naturally small size of the alveoli in the infant lung.

Gastro-enteritis or "*enteritis and diarrhea*" is a not uncommon cause of sudden death during the first year of life, although less frequent than bronchopneumonia. The symptoms preceding death may be very mild and the diarrhea slight or absent. The child vomits once or twice, may have a convulsion, and death supervenes. At autopsy this condition may be easily overlooked because any hyperemia that may have been present in the intestinal mucosa tends to disappear quickly after death. The lining of the stomach and intestines is usually pale and covered with mucus. The intestinal lymphadenoid tissue is swollen, the solitary follicles sometimes showing a black center. Occasionally the swollen solitary follicles ulcerate and form small crater-like ulcers. The mesenteric lymph glands are usually enlarged, and are either uniformly pale or uniformly pink to red on surfaces made by sectioning. The contents of the intestine of a normal infant are of a golden yellow color with an odor that is not foul. In gastro-enteritis, the contents of the small intestine are thin to watery; of the large intestine, soft and mushy, of a foul odor and often contain mucus and masses of undigested milk curds.

It has long been observed that many sudden *deaths* in children are *associated with* an *enlarged thymus gland*. Frequently there are no other gross or microscopic changes in any organs of the body that can account for the death. This condition has been designated Status thymicus, Status lymphaticus or Status thymicolymphaticus according to whether the thymus alone, or the lymph glands alone or both together are enlarged. The term lymphatic constitution has also been applied to this condition.

Usually some slight injury, such as a slight blow or a sudden physical shock, such as falling into cold water, immediately precedes the death. Occasionally emotional disturbances may be the inducing factor. Of great practical importance is the fact that the death of such individuals frequently follows a surgical operation, even a minor one, such as pulling a tooth; or they succumb to the anesthetic, death usually occurring just as they are beginning to recover from its effects. The injection of diphtheria antitoxin or of salvarsan is a not uncommon exciting cause of death in such persons. In a still smaller number of cases the child, in apparently perfect health, suddenly drops dead without any discoverable exciting cause.

In practically all of these cases, post-mortem examination reveals an enlarged thymus gland and general hyperplasia of the lymphadenoid tissue of the body. Occasionally there is only the lymphadenoid hyperplasia. The thymus gland is present at birth, increases in size until puberty, and then undergoes a normal involution by which it entirely disappears about the age of 25, its place being taken by fat. The weights and dimensions of the thymus that have been considered normal for different ages have varied with different investigators. The figures of v. Sury given in the following table appear to be the most reliable in that they are based upon glands removed from 200 well-nourished children, most of whom had died from some acute infection.

Age	Thymus			
	Length, centimeters	Breadth, centimeters	Thickness, centimeters	Weight, grams
Newborn	0.6	5.5	1.1	14.4
1 month	5.8	5.2	1.4	15.9
2 to 9 months	7.4	5.6	1.5	24.3
9 months to 2 years	7.5	5.7	1.4	23.2
2 to 14 years	9.7	6.1	1.3	25.8

Hammar's average weights are as follows:

Newborn	13.26 gm.
1 to 5 years	22.98 gm.
6 to 10 years	26.10 gm.
11 to 15 years	37.52 gm.
16 to 20 years	25.58 gm.

In children the thymus may undergo hyperplasia so that its size and weight are two or more times the normal. Schridde mentions a thymus that weighed 80 gm. The hyperplasia may affect both the cortex and the medullary portion of the gland; but more frequently the latter alone is involved. The cells of the medulla are increased in number and size; and the Hassal corpuscles are larger than normal and are composed of a fat-containing mass without nuclei. The cortex, in these cases, is thinner than normal, but not otherwise changed. The shape of a hyperplastic thymus may not be altered. On the other hand, it may have a more spherical or plumply oval shape with a very material increase in thickness. In some instances grooves are present where the thymus presses on the trachea or aorta or other vessels. Occasionally the trachea has been found flattened antero-posteriorly; and in a few reported cases there was an apparent stricture of the aorta with dilatation of the proximal portion.

Usually the lymph glands of the body are also enlarged. This applies to the mediastinal, mesenteric and retroperitoneal glands more than to the superficial ones. Of the latter, the cervical group are more frequently involved. The lymphadenoid tissue of the intestines is commonly found to be markedly hyperplastic. Peyer's patches, and the solitary follicles of the small and large intestines are very greatly enlarged; the former appearing as corrugated plateaus 1 to 2 mm. in height. Localized accumulations of lymphadenoid tissue with germinal centers are usually found in the bone marrow. Similar accumulations of lymphoid cells are seen in sections of the liver, kidneys and lungs. The spleen is enlarged, but usually only moderately; and the splenic corpuscles are much increased in size.

The heart is not infrequently found to be enlarged. This affects the left ventricle chiefly; its wall is thickened and its cavity frequently dilated. Sometimes localized lymphoid infiltration of the myocardium is present. The circumference of the aorta is commonly considerably less than normal, and its wall is thinner. The adrenal glands are often found to be very thin, the diminution in size being due to an abnormally small amount of medulla.

The problem of the mechanism of the so-called thymic death has not been solved. Many pathologists dispute its occurrence. Certain it is, that very careful search at autopsy and microscopic examination of the tissues, will very frequently reveal an unsuspected bronchopneumonia, gastro-enteritis or some other pathologic process to account for and explain the sudden death. It should be remembered that lymph glands may become enlarged from a great variety of causes; for example, the hyperplasia of the mesenteric glands in enteritis. For these reasons a diagnosis of "thymic death" should only be made when an enlarged thymus is present and after every other possible cause of death has been excluded by the most painstaking gross and microscopic examination.

However, there is a small group of sudden deaths in which no other etiologic factor can be found and the medico-legal expert is compelled to give Status thymico-lymphaticus (or lymphatic constitution) as the cause of death. Two theories, the mechanical and the toxic, have been advanced to explain the influence of the thymus in causing sudden death.

According to the mechanical theory, the enlarged thymus presses upon adjacent important structures and interferes with their function. Compression of the trachea might cause death from suffocation. This tube has been found definitely flattened in many cases. Furthermore, many of these children die while asleep on their backs, the position most favorable to compression of the trachea by an enlarged thymus. In many of these cases there is evidence of death from suffocation in subpericardial and subpleural hemorrhages. However, in other cases, no sign of pressure on the trachea and no evidence of suffocation are to be found. Instead, the manner of death and the dilatation of the heart indicate a cardiac death. For this reason pressure on the vagus nerve, or on the great vessels (aorta, superior vena cava and pulmonary vessels) or mechanical interference with the auricles of the heart itself, have been offered as explanations of "thymic death." Hyperthymization by some toxic substance suddenly liberated in excess from the enlarged gland has also been advanced as the cause of these sudden deaths. Symmers considers thymic death as the result of some explosive action similar to anaphylactic shock. The toxic theory has little in the way of substantial proof in its favor, and yet it explains more of the phenomena of many of these cases than does the mechanical theory. For the present we must admit that no adequate explanation of the mechanism of thymic death has been offered.

Finally, it should be emphasized and repeated that the utmost caution should be used in making this diagnosis. Status thymicolymphaticus should only be given as the cause of death when the essential lesions which characterize this condition are present, and after every other possible cause has been excluded by a most exhaustive gross and microscopic examination.

Asphyxiation of very young infants may result from the child's turning upon its face on a soft pillow or from getting the cover over its mouth and nose. In older children asphyxiation may result from rupture of a retropharyngeal abscess or of large caseous peribronchial lymph-nodes into the upper air passages. Other, even more rare conditions, such as lodgment of bolus of food in the larynx, also cause death by asphyxiation. Laryngospasm is only very rarely a cause of sudden death in children. The post-mortem findings in cases of death from asphyxiation have already been sufficiently discussed. It is necessary to examine carefully for the cause of the asphyxia.

Children suffering from *marasmus* are not infrequently found dead. Sometimes a lowering of body temperature is the immediate cause of death. But in a certain number of such cases, as Holt remarks, "the vital spark simply goes out after burning for some time with a feeble intensity." No very characteristic changes are found at post-mortem except the extreme emaciation.

Internal hemorrhages are rare causes of sudden death in children. Many of these are traumatic in origin, the injury occurring during birth or afterward. Intracranial hemorrhage is not very uncommon after prolonged labors. Spontaneous hemorrhages into the lungs or into the peritoneal cavity occasionally occur. Merkel collected four cases of spontaneous rupture of the aorta and four of similar rupture of the heart in children under 15 years of age. Bilateral extensive hemorrhage into the adrenals occurs in rare instances, as in the case of a three-year old boy, seen by the author. There were extensive hemorrhages into all organs, but each adrenal was reduced to a pulpy mass densely infiltrated with blood and surrounded by the capsule of the gland. This child died after being ill for about six hours.

Acute general *peritonitis* may follow a latent appendicitis, and cause death within a few hours. If the attack comes on soon after a meal, poisoning may be suspected.

Death from suffocation may terminate a laryngeal *diphtheria.* Sudden failure of the heart may develop some time after the primary lesion of diphtheria has disappeared. In such cases the heart may either be very soft and flabby; or it may be in systole, but the muscle is mottled with yellowish areas which, on microscopic examination, are found to be foci of fatty degeneration. Deaths from this cause may acquire medico-legal importance because of the suddenness with which they occur, frequently at a time when the child is apparently in perfect health.

Lesions of the brain may require medico-legal investigation. *Meningitis* may be primary, or be secondary to trauma, otitis media, etc. Careful examination and keen judgment may be required if the inflammation of the meninges develops soon after a bodily injury, such as corporal punishment, a blow on the head, etc. Usually pus is sufficiently abundant over the upper part of the brain to make a diagnosis at necropsy possible. In very virulent streptococcus infections, however, the gross changes may be limited to a very slight hyperemia of the meninges. Richter has called attention to the results that may follow *too early closure of the sutures and fontanelles.* The continued growth of the brain may make it possible for an otherwise moderate edema of the brain to cause death.

Von Gierke has advanced the idea that partial asphyxiation during birth induces hemorrhages into the parathyroid glands. This, in turn, is the source of a tetany that may prove fatal. Others, for example, Haberfeld, believe that some cases of tetany originate thus. Merkel does not accept this as fully demonstrated.

SUICIDE IN CHILDREN

"Evidence is not wanting that suicide among children is on the increase in this as well as in other countries." Increase of this crime in Germany and France had become so great that an extensive literature concerning it had grown up in these countries prior to 1914. Practically no studies of suicides in children appear to have been made in the United States. Hoffman believes that it is more common here than is generally assumed; and that tendency to error in diagnosis and falsification of death certificates are more pronounced than at older ages.

In France in 1897 there were 76 suicides in children under 15 years of age, as follows: 15 years old, 37 cases; 14 years, 24 cases; 13 years, 9 cases; 12 years, 2 cases; 11 years, 4 cases.

Redlich and Lazar analyzed 44 suicides and 17 attempted suicides in children as follows;

Age, years	Suicides		Attempted suicides	
	Boys	Girls	Boys	Girls
3	1	0	0	0
4	0	0	0	0
5	0	1	1	0
6	0	0	0	0
7	0	0	1	0
8	2	0	0	1
9	1	1	1	0
10	1	0	1	0
11	4	1	2	0
12	0	4	2	2
13	3	3	0	2
14	1	2	1	1
15	4	3	0	1
16	6	6	0	0
Total	23	21	10	7

In Bavaria between 1903 and 1907, 37 suicides were reported in children under 15 years and 295 in youths between 15 and 20 years old, as follows:

Year	Total number of suicides	Suicides in children		
		Up to 10 years	11 to 15 years	16 to 20 years
1903	937	0	7	60
1904	880	0	9	51
1905	850	0	5	55
1906	894	0	9	55
1907	979	0	7	74

In the Registration Area of the United States for the five year period 1915 to 1919, there were 165 suicides in children under 14 years of age and 1661 in youths between 15 and 19 years old. The analysis of these cases is shown in the following table:

Year	Suicides					
	Under 10 years		11 to 14 years		15 to 19 years	
	Boys	Girls	Boys	Girls	Boys	Girls
1915	0	1	19	17	154	204
1916	1	0	20	11	187	193
1917	0	0	13	9	140	162
1918	0	1	19	18	150	157
1919	0	0	24	12	162	152
	—	—	—	—	—	—
	1	2	95	67	793	868

From the statistics cited in the above tables it is seen that suicide in children under 10 years of age is extremely rare. The relative number of such deaths, compared with the total number of suicides under 15 years of age, varies, however, in different statistical groups. Thus in the series studied by Redlich and Lazar, of 25 suicides under 15 years of age, 6, or 25 per cent., were under 10. In the Registration Area of the United States for the 10 year period from 1904 to 1913, of 239 suicides among children under 14 years old, only seven (about 3 per cent.) were under 10. In the same Area for the five year period from 1915 to 1919, only three (about 2 per cent.) were under 10 years old out of a total of 166 under 15.

The influence of sex in suicide rates in the early age period as compared with the same rates for later periods is shown in the above and in the following tables. Under 14 years, suicides are more frequent among boys than girls, in about the proportion of 14 boys to 10 girls. Between 15 and 20, the number among girls slightly exceeds those among boys, in the proportion of about 90 males to 100 females. The general suicide rate for all ages is about three men to one woman. In European countries the proportion of suicides among boys is higher than in the United States. In France the rate is about three boys to one girl; in Germany and Russia, four or five boys to one girl.

Table 1 is an analysis of methods employed in 165 suicides in children and 50,701 suicides of all ages in the Registration Area of the United States for the five year period 1915 to 1919. The total number of suicides under 14 years is relatively small and any conclusions based upon an analysis of these figures are admittedly less exact than are the deductions from a study of the larger number of suicides among adults. In the order of frequency employed the methods of suicide in children are hanging, firearms, poison and drowning; while in adults the order of frequency is firearms, poison, hanging and asphyxiation. The percentages of suicides by hanging and drowning in children are nearly twice the percentages for the same methods in adults.

TABLE 1.—SUICIDES

Method of suicide	Under 16 years						All ages					
	Males		Females		Total		Males		Females		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Poison	10	10	25	36	35	21	5,326	14	4,035	32	9,361	19
Asphyxiation	6	6	6	9	12	7	4,416	12	2,648	21	7,064	14
Hanging or strangulation	42	43	6	9	48	30	6,589	18	1,608	13	8,197	16
Drowning	4	4	12	18	16	10	1,960	5	1,273	10	3,233	6
Firearms	30	33	17	25	47	28	15,110	39	1,805	14	16,915	33
Cutting or piercing instruments	1	1	0	0	1	0.6	3,109	8	429	3	3,538	7
Jumping from high places	1	1	1	1	2	1.1	832	2	549	4	1,381	3
Crushing	1	1	0	0	1	0.6	373	1	101	1	474	1
Other suicides	1	1	2	2	3	1.7	290	1	248	2	538	1
	96	....	69	....	165	....	38,005	....	12,696	....	50,701	....

Differences in methods used by the two sexes are more striking than among adults. Thus, of 48 suicides by hanging 87 per cent. were boys and 13 per cent. girls; while among adults 80 per cent. were men and 20 per cent. women. Of 36 juvenile suicides by poison 72 per cent. were girls and 28 per cent. boys; of the adult suicides by this method 43 per cent. were women and 57 per cent. men. Of 47 suicides by shooting 64 per cent. were boys and 36 per cent. girls; while nearly 90 per cent. were men and 10 per cent. women. Drowning is a more common method of suicide among girls (75 per cent.) than among boys (25 per cent.). Among adult suicides by drowning 60 per cent. were men and 40 per cent. women.

Methods of committing suicide employed by children in other countries differ slightly in their order of frequency from those used in the United States. Thus Redlich and Lazar classified their 61 cases of suicide and attempted suicide in children as follows:

	Males	Females	Total	Per cent.
Poison (including asphyxiation by CO gas)	4	7	11	20
Hanging or strangulation	8	1	9	14
Drowning	5	4	9	14
Firearms	4	3	7	11
Cutting and piercing instruments	2	0	2	3
Jumping from high places	7	12	19	31
Crushing (allowing vehicle to run over one)	2	1	3	5
Other suicides	1	0	1	2
	33	28	61	

In this series of cases the order of frequency of method employed was jumping from high places, poison (including asphyxiation), hanging and drowning.

No studies of motives leading to suicides in children has been made in the United States. Siegert analyzed 57 cases of suicides in children up to the age of 16, and classified them according to motive as follows:

	Boys	Girls	Total
Fear of punishment	19	7	26
Grief	6	4	10
Injured sense of honor	7	3	10
Mistreatment	4	1	5
World weariness	0	6	6
	—	—	—
	36	21	57

Baer studied 25 cases and concluded that about 50 per cent. were due to fear of punishment.

The most extensive study of motives for suicide is that of Chlopine based on 1117 cases. These were classified as follows:

Fear of punishment	336 cases
Unwillingness to attend school	8 cases
Fear of failure on examination or of failure of promotion	52 cases
Expulsion from school	6 cases
Mental work	2 cases
Other causes associated with school	20 cases
Corporal punishment at home or at school	9 cases
Unjust treatment by parents or teacher	26 cases
Anger, obstinancy, etc	13 cases
Love affairs	21 cases
Mental diseases (insanity)	70 cases
Melancholia	30 cases
Morbid sense of honor	37 cases
Excessive ambition	25 cases
Motives unknown	321 cases
Miscellaneous motives	141 cases
Total	1117 cases

Eulenberg, from his study of a series of suicides in children, concluded that in 48 per cent. of cases the motives were connected with school work; in 28 per cent. there was a neuropathic predisposition; and that 24 per cent. of these suicides resulted from miscellaneous causes. It appears, therefore, that a very large percentage of suicides in children grow out of maladjustments in school. Failure of parents to understand their children, and to recognize that they are moved by much the same passions—anger, jealousy, desire for revenge, etc.—

as are adults, is a fruitful source of juvenile suicides. The humiliation incident to knowledge of illegitimacy or to divorce of parents or family disgrace in general has led many sensitive children to take their own lives. The Freudians assume that masturbation is in some way concerned with the majority of juvenile suicides.

Suicides among children are much more common in cities, especially the larger ones, than in the country. This is probably due to the more natural and healthy life of childhood in the country as compared with the artificial and abnormal life of children in cities. Suicides in children are less deliberate than those in adults, and are therefore more likely to result from a momentary passion, such as extreme anger, or the shock of sudden humiliation.

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CHAPTER CXCIII

TUMORS OF INFANCY AND CHILDHOOD

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PART I. GENERAL BIOLOGY OF TUMORS

Definition.—The formulation of a definition of tumor, which will be at the same time both inclusive and exclusive enough, is a matter of such extreme difficulty in the case of tumors of adults that none of the definitions of the master pathologists has received universal acceptance. In the neoplasms of children, the inability to make a sharp and satisfactory differentiation between malformation and tumor adds to the difficulty. A definition should be limited to a statement of those characteristics which establish the nature of tumor and which, being characteristic, apply to tumor alone, as opposed to other pathologic processes. Many so-called definitions concern themselves with speculations as to the origin of tumors and as to the biologic processes which take part in their formation. The definition must, of course, be influenced by such considerations. It is, perhaps, the lack of precise knowledge of factors relating to the initiation of tumors which makes a satisfactory definition of what actually is meant by tumor so difficult.

The generic term itself, which we apply to the lesion under discussion, is faulty and fails us in even some of our most fundamental conceptions. If we prefer "tumor," we are forced to admit at once that swelling is an attribute of many lesions which are not tumors and, conversely, that a group of metastatic tumor cells so small that it does not cause swelling is yet undoubtedly a tumor. If we prefer "neoplasm" for the thing itself and "neoplasia" for the process, then again we are confronted by the fact that a new formation of tissue is just as characteristic of regeneration or of hyperplasia as it is of tumor formation; and, on the other hand, in the case of some of the congenital tumors of children, it is possible that the neoplasm is no newer than the individual who bears it, if one may accept the origin of tumors from one of the group of blastomeres which give rise to the individual. The coining of a new, supposedly definitive, word like "blastoma" does not help us, because it simply substitutes the Greek -oma for "tumor" and hints at the origin of the structures in the first syllable of the word, being in the latter respect not broad enough to include all those structures which we properly group under the neoplasms.

It might be the part of wisdom to attempt no definition whatever, and to leave to the inner consciousness of the individual the conception of what is meant by a tumor. How difficult this apparently simple matter of arriving at a satisfactory definition actually is, becomes apparent from those definitions which have been made. Cohnheim[1] defined tumors as circumscribed atypical productions of tissue from a matrix of superabundant or erratic deposit of embryonic elements. Ziegler[2] said: "a tumor is a new formation of tissue possessing an atypical structure, not exercising any function of service to the body, and presenting no typical limit of growth." For von Rindfleisch[3] a tumor was a localized degenerative excess of growth. Birch-Hirschfeld[4] defined tumors as originating spontaneously, becoming separate from the physiologic tissues in their physiologic and functional relationships, developing from the cells of the body, and possessing progressive growth. Ribbert[5] said tumors are self-confined, dependent upon the organism for their nourishment, but otherwise largely if not quite independent, corresponding more or less but never absolutely with the tissues of the natural body, and presenting no definite limit to their growth. Lubarsch:[6] Under tumor proper we have to understand those growths of apparently independent origin which histologically correspond in structure more or less completely with the matrix from which they originate, but in form are atypical; which further, in spite of their organic connection with that matrix, and in subjection apparently to laws of their own, pursue an independent existence which is not, or only exceptionally of advantage to the organism as a whole. Borst[7] defined tumor formation as a local, purposeless, autonomous overgrowth of cells and tissues, which arises without known cause, and which leads to the formation of a product which is morphologically and biologically more or less atypical. Prudden[8] said tumors "are in general characterized by such independence and by such irregularity in growth both in structure and extent; by such a lack of relationship to the functional requirements of the individual; by such an emancipation from that subtle physiologic restraint which limits cell growth and proliferation in the normal body, and in the new tissue formation in repair, that their distinguishing character is perhaps best indicated by the word autonomy, or by the more striking suggestions of the term cell-anarchy." Mallory[9] says "a tumor is a new formation (usually a more or less circumscribed collection) of cells which proliferate continuously and without control; tend to differentiate as the cells from which they arose would do under normal conditions; serve no useful function; lack an orderly structural arrangement; and have at least at the present time no assignable cause for their existence." Adami[10] prefers C. P. White's[11] statement that "a tumour proper is a mass of cells, tissues or organs, resembling those normally present in the organism, but arranged atypically, which grows at the expense of the organism without at the same time subserving any useful function therein."

In the above conceptions of tumor, a number of the more striking properties are emphasized. The one which is stressed heavily and finds itself expressed in one form or another most frequently, is the independence of tumor tissue from the mechanisms which control the reproduction and growth of normal tissues. This striking and unexplainable attribute has been well named autonomy. Since it is the one common and most outstanding feature of tumors, perhaps Ewing's[12] succinct definition, "a tumor is an autonomous new growth of tissue," is most acceptable. All the various attributes of tumors cannot be included in a definition; the more striking ones require a certain amount of more detailed consideration.

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GROWTH OF TUMORS

Since autonomy is the most striking characteristic of tumors and is an expression of the growth phenomena of neoplastic tissue, growth becomes one of the most important attributes of tumors. Autonomy is, first of all, an evidence of independence of tumor tissue from the rest of the body. This independence is, however, only relative. Tumors, like other tissues, must derive their sustenance from the body fluids, and to this extent they are dependent upon the rest of the body. But given a vascular supply which is adequate for nutrition, tumors seem not to be controlled by the biologic laws which govern the growth of normal tissues. This freedom of control is best illustrated by those tumors which grow rapidly at the expense of the rest of the body, the latter undergoing progressive wasting whereas the tumor continues to grow.

Slow Growth.—Although the two phenomena are mutually interrelated, we must distinguish between the growth of a tumor as a whole and the growth phenomena exhibited by its constituent cells. Some neoplasms increase in size very slowly, often so slowly that the increase becomes perceptible only through careful measurements; such tumors may, in fact, finally cease to increase in size. In such slowly growing or stationary tumors, new accessions of growth energy may occur at some later period from causes not yet determinable, so that even tumors of this type carry within themselves the potentialities of lawless growth.

Slow growth is often associated with reaction upon the part of the surrounding normal tissues, a reaction which may lead to encapsulation of the tumor by a fibrous membrane of considerable thickness. If the growth of such slowly progressing neoplasms is correlated with the morphology of their cells, as determined by microscopic study, one is struck at once by the differentiation of the cells, that is, by their close morphologic approach to ripe tissues of the kind from which the tumor cells have been derived. A subcutaneous fibroma, a lipoma, or a uterine fibromyoma may be composed of tissue so similar to fibrous or adipose tissue or uterine muscle as to make it difficult to say that one is dealing with a tumor if one has only a small section for examination. There are usually slight deviations from normal in the arrangement of the cells with regard to one another, in the distribution and character of the blood-vessels, and in the size of the cells, which may arouse suspicion, but these deviations need not be so great as they are in regenerating tissues. The cells of slowly growing tumors of the connective tissue group may form intercellular derivatives not to be distinguished morphologically or chemically from those of normal tissues, and the cells of slowly growing glandular tumors may exhibit evidences of secretory activity. In these tumors, the rate of growth is such as to permit not merely complete or almost complete morphologic differentiation, but also a certain degree of functional activity. The latter, however, can apparently subserve no useful function for the body as a whole.

If we attempt to correlate the growth phenomena of a slowly growing tumor as a whole with the evidences of growth and multiplication of its constituent cells, then we find that the cells throughout the tumor are usually uniform in appearance and are of equal age, as determined by the degree of differentiation present. The cells appear to multiply at the same regular rate throughout the tumor mass, so long as nutritional conditions are equal throughout the tumor. The growth of slowly growing tumors is, therefore, said to be universal, central or expansive. It results in a more or less regularly spherical mass, if the resistance offered by the surrounding tissues is uniform on all sides, or in a flattened and irregular mass, if the restraint is unequal. The general rule that growth is uniform throughout the mass of slowly growing tumors has exceptions in those tumors whose cells are formed by the blastogenic activity of a particular portion or zone of the tissue. Thus, cartilaginous tumors or chondromas increase in size by peripheral growth and by accretions upon the surface of the mass from a surrounding perichondrium. Of the utmost clinical importance is the well established fact that a tumor which has grown slowly for years may suddenly begin to grow at a much more rapid rate, a change which is associated with an entire reversal of the characters of the neoplasm. The cause of such a sudden accession of growth energy cannot be determined. It might, theoretically, be the result of an increase in the activity of the same growth incitants which initiated or maintained the previously slow growth; to the addition of new and different incitants acting with greater intensity than those to which the tumor had previously been subjected; or to changes within the cells themselves, which make them answer by more rapid multiplication to those factors previously at work. Mere increase in nutrition does not appear to be a factor of importance in this phenomenon.

Rapid Growth.—In other tumors, growth proceeds at such a rapid rate that increase in size is readily perceptible. Such rapid growth tends to be associated with poor peripheral definition of the tumor and with union of the tumor tissue to surrounding structures. Microscopically, the latter characteristics are seen to be due to absence of a capsule and to active invasion of the surrounding tissues by strands of tumor cells.

In rapidly growing tumors growth is said to be peripheral. Active multiplication at the periphery is, in fact, quite evident, but the application of the term peripheral to the growth phenomena of rapidly growing tumors must not be understood to mean that multiplication of cells at the center of the mass has ceased. If the nutrition of deeper areas is not interfered with, the cells here also undergo rapid proliferation. While it is not strictly exact, therefore, to intimate that growth does not occur throughout the mass, it is at the periphery that rapid growth reveals its most striking characteristic, namely, invasion of surrounding tissues at such a rate that reaction upon the part of the latter does not lead to encapsulation. Because of the lack of restraint, such tumors are apt to be more irregular in shape than slowly growing ones; growth occurs out into the surrounding structures along the paths of least resistance, the resulting irregularity and poor definition of outline being reflected in the names "cancer" and "*Krebs*," which have been applied to such tumors. Formation of neoplastic tissues may proceed at such a rate that the mixed tumor of the kidney may already have reached such a size before the birth of the child that delivery is interfered with; or in a tumor of the liver of a child, the involved organ may reach such dimensions that it weighs more than the rest of the child. Furthermore, while rapid growth may lead to the formation of a large amount of tumor tissue at the primary focus, it also frequently results in the formation of secondary tumor nodules distant from the original site, the phenomenon of metastasis to be considered below.

Rapidity of growth is associated not only with the gross characteristics which have been stated, but also with striking absence of differentiation of the tumor cells to be detected microscopically. The undifferentiated, immature and atypical character of rapidly growing tumor cells is in marked contrast to the differentiated, mature and typical nature of the cells of slowly growing tumors, and is the one feature from which the microscopist draws his conclusions as to the nature of the tumor, which are of such paramount clinical importance. The immaturity of the tissue manifests itself both in the condition of the cells and in their relationships to each other, the arrangement of the cells deviating from that which is characteristic of the normal tissue from which the tumor is derived.

DIFFERENTIATION, ANAPLASIA AND METAPLASIA

Differentiation.—The process which manifests itself by lack of differentiation has led to much speculation, which seeks to elucidate some of the most fundamental properties of tumors. It may be stated almost as a law, that the more rapid the growth of a tumor, the more undifferentiated are its cells. The converse is also true, and from the degree of differentiation present, the microscopist is able to determine whether a given tumor was a rapidly or a slowly growing one. Do the cells fail to differentiate because their rate of multiplication is such that there is not time for differentiation between successive cell divisions? Or do the cells multiply rapidly because they have lost the power to differentiate? These questions raise two distinct possibilities which are of fundamental importance in arriving at an understanding of the biologic processes active in tumors.

In certain of the normal tissues, the replacement of cells lost by ordinary wear and tear, and the regeneration of cells following the action of injurious agents, are brought about by the multiplication of incompletely differentiated, slumbering "mother" cells. In most tissues, and especially in those which are most active in repair, it is apparently the differentiated and functioning cells which must multiply; the Grawitz theory of slumbering connective tissue cells, from which new cells are derived, probably does not deserve acceptance. If normally differentiated cells must proliferate to form new cells, the phenomena which must occur in such cells antecedent to division are important. That a completely differentiated cell, no matter of how low a functional order, can go into division as such appears improbable. The work of R. Hertwig[1] and his school indicates that division requires certain definite volume relationships between nucleus and cell body. The nucleus-plasma relation necessary for division is not such as exists in differentiated cells; the latter must undergo a certain degree of dedifferentiation, followed by disproportionate growth upon the part of cytoplasm and nucleus, before the divisional tension is reached. In normal tissues, dedifferentiation and growth which lead to multiplication appear to be influenced or initiated by the loss of mutual restraint, which cells normally exercise on each other, when one or more of a group disappears, either through physiologic death or through injury. Loss of differentiation and a return to an immature state is a prerequisite for division in normal tissues.

Following the above reasoning, the same process would appear to be a primary one in all tumors. Cellular multiplication, even in slowly growing tumors, must be associated with loss of differentiation upon the part of those cells whose increase in number leads to growth of the tumor, no matter how slight the latter may be. But even if we grant that cells must become undifferentiated before they can give rise to tumors, we have no explanation of the fact that in certain tumors differentiation occurs and is associated with slow growth, whereas in other tumors it does not occur and the loss of differentiation is associated with rapid growth. Those biologic laws which restrain the unlimited proliferation of normal tissues appear to be in abeyance in tumors. In normal tissues, multiplication ceases when the incitant to division has been overcome or when the necessary repair has been made. It may be that the thing which gives to tumor tissues their autonomy is a continuously acting incitant to division; depending upon the degree of action of such incitants, growth might be slow or rapid. This, of course, is speculation; we know little or nothing of factors which incite tumor growth, and hence we are unable to determine whether such factors need to act merely at the initiation of the neoplasm or continuously throughout its later life history.

It is conceivable that the tumor incitant needs to act only once and only for a brief period, producing the first generation of cells, whose descendants later grow lawlessly to form a tumor. The cells originally acted upon may be abnormal, in that the balance between divisional and functional energy may be upset in the resting cells; or the descendants of normal cells may emerge from a divisional stage, induced by a momentarily acting tumor incitant, with a disturbed balance. Such a conception has a certain amount of morphologic support in those protozoan cells whose divisional and functional energies are controlled by morphologically distinct nuclear entities. If we might postulate a similar condition of nuclear duality for metazoan cells and might suppose that the divisional activities of cells are controlled by certain nuclear elements, whereas the somatic activities, which manifest themselves by differentiation and function, by still other elements, then the loss of somatic chromatin in varying degree would help to explain some of the phenomena which occur in tumors. By such a process, cells would lose, in some cases slightly and in other cases more completely, the potentiality for differentiation and function.

Anaplasia.—The loss of the morphologic attributes of maturity is such a striking character of the cells of rapidly growing tumors, that such cells are often referred to as being embryonic in type. That they are immature must be granted, but that they are embryonic cells, in the strict sense of the term, is not true. They have lost one property which is most characteristic of normal embryonic cells. The destiny of the latter is to differentiate, after a variable number of divisional generations, to become mature, and to function. It is just these properties which the tumor cell has lost. Adami[2] has expressed what occurs, in the statement that tumor cells have lost the habit of function and have taken on the habit of growth. While this is an apt statement of what occurs, it leaves us in the dark as to the why and the wherefore of the process. It conveys the intimation that tumor cells remain immature and do not differentiate because they have lost the property of differentiation. The writer is inclined to believe that the latter is a truer statement of conditions, than that tumor cells do not differentiate simply because they multiply rapidly. Rapid multiplication would appear to be the result of loss of power to differentiate, rather than the cause of the latter phenomenon. This view is in accord with that of Hansemann,[3] who looks upon dedifferentiation, to which he has applied the term anaplasia, as a fundamental characteristic of tumors, upon which the growth of the latter depends.

Anaplasia expresses itself not merely in immaturity of the cell, but also in other morphologic evidences of biologic deviation from the normal. R. Hertwig[4] has shown for certain protozoan cells, when divisions follow each other in rapid succession or when conjugation is prevented, that these cells fall into an abnormal physiologic state which he termed depression, characterized chiefly by hyperchromatism and disturbances of the normal nucleus-plasma relation. The condition of depression may be overcome by processes which restore the normal relation. When this occurs, the cell is rejuvenated and its life is spared or prolonged.

Howard and Schultz[5] have shown that cells of rapidly growing tumors also give morphologic evidence of states of depression, such as hyperchromatism, excessive nuclear size, and degenerative processes within the cells, which are the result of depression. Of greater importance, is their belief that the tumor cell makes use of a variety of mechanisms for overcoming depression not used by normal cells. Extrusion of nuclear chromatin, nuclear budding, and multipolar mitoses are looked upon as the morphologic expression of biologic processes which the tumor cell uses to overcome the depression into which it inevitably falls as the result of its rapid multiplication. These processes restore a nucleus-plasma relation which permits cell division. They help to maintain a division rate which is associated with lack of differentiation. That these processes are not effective in every cell is evidenced by the striking proportion of cells, in every rapidly growing tumor, which degenerate and die. The growth of such tumors is maintained by relatively few cells which are able to overcome their depression and to continue to multiply. Schultz,[6] in a study of the abnormal mitoses of tumor cells, has sought to correlate these mitoses with the more primitive divisional mechanisms of lower orders of cells. With the assumption of primitive divisional mechanisms and of processes which permit the overcoming of depression, the tumor cell has become transformed into a cell of a biologic order entirely different from any normal cell, either embryonic or adult, with which we are familiar. It is the elucidation of the peculiar and abnormal biology of the tumor cell itself, which should and must constitute the fundamental problem of tumor research, rather than the search after hypothetical tumor incitants. The experimental production of true tumors by the action of chemical agents, now an established fact, offers the hope that it may be possible to follow the succession of changes through which the normal cell passes in its transformation to a tumor cell and to interpret the biologic phenomena which make the cell a tumor cell.

Metaplasia.—The development, within a tumor, of tissue of a type different from that of the normal matrix, in which the tumor occurs and from which the tumor may be assumed to have arisen, is not an infrequent occurrence. When this happens in an embryonal neoplasm, of the kind to which the term mixed tumor is applied because of the variety of tissues which may be present, the phenomenon may be explained upon the assumption that the tumor has come from cells arising so early in the period of embryonic development that their derivatives still have the potentiality of forming several kinds of tissue. This assumption does not help to explain the origin of heterologous tissues in tumors presumably derived from unipotent cells of the post-embryonic period. For this phenomenon we must accept a belief in the occurrence of metaplasia, a direct transformation of tissues of one type into another type. It is to be noted that this transformation usually results in a tissue closely related to that from which the tumor originated. When metaplasia occurs, a tumor derived from a supporting tissue usually gives rise to a supporting tissue derivative closely allied genetically with the tissue from which the tumor came; similarly, metaplasia in an epithelial tumor results in the formation of a different kind of epithelial derivative, not of an entirely distinct kind of tissue.

If dedifferentiation or anaplasia has the fundamental importance in tumors that we have attached to it above, then it may be possible to explain metaplasia in tumors upon the basis of a state of anaplasia, which was reached before the transformation into a new type of tissue occurred. Granted that multiplication of tumor cells is preceded by a varying degree of loss of differentiation, then it is conceivable that varying degrees of differentiation may occur in succeeding cell generations, as does occur in the slowly growing tumors. Furthermore, we may postulate that alterations, either chemical or physical, in the environment of the developing cells, may cause them to take on the morphologic characters of a different, but closely related, cell type.

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BLOOD- AND LYMPH-VESSELS, NERVES, AND STROMA OF TUMORS

Blood-vessels.—Except in those neoplasms which are derived from and made up of blood- and lymph-vessels, these structures come from the host stroma, and are carried along with such stroma as enters into the composition of the tumor; they are not formed from tumor elements. At the advancing margin of infiltrating tumors, new formation of capillaries occurs, apparently as the result of an inflammatory stimulus exerted upon the surrounding tissue by the tumor. The peripheral tumor zone, as it invades this vascular area, may become quite vascular. In slowly growing benign tumors, there occur large vessels with the structure of normal arteries and veins; these are probably the vessels of the original tissue taken over by the tumor. In rapidly growing neoplasms, normal vessels are rarely encountered; such as are present are original arteries and veins which have not been overcome by the tumor tissue. The newly formed vessels do not go beyond the capillary stage; their walls are devoid of smooth muscle and elastic lamellæ, although the lining endothelium may rest upon a narrow layer of dense fibrous tissue. The arterioles of the surrounding host tissue break up rapidly into newly formed capillaries of the type described, and these may become dilated into sinuses of considerable size. These unite again with the surrounding veins. The circulation through rapidly growing tumors is by means of a tortuous, cavernous, atypical system, which does not appear capable of functioning, either mechanically or physiologically, like the vascular system of a normal tissue. The circulation, furthermore, is not uniform throughout the tumor, since the thin-walled vessels are subject to thrombosis, and to occlusion, obliteration and invasion by the tumor tissue. The greater the distance from the peripheral zone of anastomosis with the host circulation, the more difficult does the circulation become; this explains the great tendency of the central parts of malignant tumors to massive necrosis of the infarction type.

Whether tumors have a direct and specific formative action upon blood-vessels, other than their irritant and inflammatory action, appears doubtful. In many sarcomas, the tumor tissue is richly supplied with vessels. These at first carry along stroma, which they have received from the non-neoplastic tissue. Within the tumor, this may disappear completely, the endothelium of the vessels lying directly upon the tumor tissue. The greater richness of such tumors in vessels which are not protected against the tumor by a surrounding zone of host stroma may be the result of a formative stimulus exerted by the tumor tissue upon the vascular endothelium.

Lymphatics.—A definite and closed system of lymphatic channels is not developed in rapidly growing tumors, although wide, endothelial lined lymph spaces are sometimes fairly numerous in benign tumors. These must be original lymphatics included within the tumor, as are the large arteries and veins. Evidences of stimulation of lymphatic endothelium in the tissue surrounding invasive tumors are usually absent. Carcinomas may invade the surrounding lymphatics and grow within the latter, without evident proliferative reaction of the endothelium.

Nerves.—Except in the rare true neuromas, nerve fibers do not grow into tumors. The peripheral zone may contain a few, which have been included from the normal tissue. These undergo atrophy and disappear as the tumor increases.

The autonomy of tumors has been referred to above as one of the most striking features of neoplasia. While all the factors concerned in this independence of the tumor are not known, the relations of blood-vessels and nerves furnish striking morphologic evidence of autonomy. Although the tumor tissue must have bloodvessels in order to obtain adequate nutrition, the blood supply is not controlled as it is in normal tissues. The mechanics of the circulation must be quite different from that which obtains in normal structures, and the absence of vaso-motor nerves precludes any regulatory mechanism through which the rest of the body might control the tumor. Nerve fibers conveying trophic influences, if such may be supposed to have an effect upon the nutrition of normal tissues, are also absent. A tumor, therefore, may be looked upon as an independent structure interpolated upon a circulatory system which the rest of the body can not control, but which serves as a path of nutritional supply to the tumor, and as a path by which the tumor may return its own metabolic and degeneration products to the body to act harmfully upon the latter. It is an arrangement which leaves the altruist and the teleologist aghast.

Stroma.—The supporting framework or stroma of tumors is probably derived largely from the original tissue within which the neoplasm develops. In the case of the epithelial tumors it comes entirely from the pre-existing stroma. The original parenchymatous elements of the occupied territory disappear through compression and atrophy, the tumor cells infiltrating themselves into the spaces between the supporting elements thus vacated. This taking over of the original stroma by an epithelial tumor may be associated with only very slight reaction upon the part of the connective tissue itself, in the case of many of the benign tumors; the stroma appears to play a passive rôle, tending only to encapsulate the tumor at its periphery. In the benign papillary epithelial growths, proliferation of the supporting tissue may be as active as that of the covering epithelium; as a matter of fact, in many such papillomas one gains the impression that stroma proliferation was the primary process, epithelial proliferation occurring secondarily to keep pace with the multiplication of the underlying tissues. In most of the epithelial neoplasms of more rapid and invasive growth, the stroma reacts in characteristic fashion. It becomes dense, acellular, often hyalin, and appears to be not only relatively but actually great in amount. Depending upon the relative proportions of stroma and of epithelial tumor tissue, such neoplasms may be scirrhous or medullary in type, in the former the stroma being relatively prominent, and in the latter the tumor tissue predominating. But even in the latter, the large islands of cellular tumor tissue may be separated by bands of connective tissue which exhibits the characteristic reactions of condensation and hyalinization. The reaction of the stroma to the presence of carcinoma appears to be the result of a stimulative action of the latter upon the former, and appears also to be a protective mechanism upon the part of the host tissues, whose aim is the restraining of the growing tumor. That the stroma is not entirely passive in a carcinoma, that it does not merely appear prominent only as the result of the loss of the original parenchymatous elements, and that it actually increases in amount, is well shown in the axillary lymph-node metastases of mammary carcinomas. In such nodes the lymphoid tissue, which normally contains a minimal amount of supporting tissue, may be transformed, in the presence of metastasis, into a densely fibrous and hyalin tissue often as prominent as in the primary neoplasm. Such an amount of stroma can result only from actual multiplication of the pre-existing supporting tissue of the lymph-node. Although actual multiplication must occur, it proceeds at such a rate that there is time for complete differentiation or the carcinoma cells stimulate the connective tissue to a rate of differentiation which is more rapid than that of inflammatory or regenerating stroma. One of the striking characteristics of many carcinomas is the presence of actively growing, undifferentiated epithelial tissue embedded in completely differentiated, fibrotic stroma.

In the tumors derived from the supporting tissues themselves, the relation of the tumor elements to the original stroma is not readily determined, nor is it possible to say with certainty how much of the stroma present is derived from the original framework of the tissue and how much has been formed by the tumor elements. Probably at the beginning such neoplasms also appropriate the pre-existing stroma, as do the epithelial tumors. But since the tumor parenchyma is derived from tissues which have the property of forming intercellular ground substance, the tumor cells themselves may differentiate sufficiently to form supporting tissue. Such stroma of neoplastic origin is not to be distinguished from that derived from the original tissue. In the rapidly growing sarcomas, the stroma probably all comes from pre-existing supporting tissue, as in the carcinomas, but it exhibits a striking difference from that of epithelial tumors of equal rapidity of growth. In the sarcomas, the stroma forms a relatively minor part of the tumor tissue, and it remains immature. The stimulus to differentiation appears to be absent, although the greater amount of stroma formed in a carcinoma would seem to necessitate as a great a degree of proliferative activity in the carcinoma as in the sarcoma.

INVASION

Another manifestation of the lawless growth of tumors is invasion of the surrounding normal tissues. This process is one of extreme importance for the body as a whole, and results in the overcoming of the body by the tumor. It is a result of the rate of multiplication of the tumor cells in the peripheral portions of rapidly growing neoplasms. The newly formed cells insinuate themselves into tissue spaces and lymphatics, growing along these paths of lesser resistance. As a result, the original tissue elements are compressed, undergo degeneration and atrophy, and finally die and disappear. There occurs in this way a gradual, progressive and continuous encroachment of the tumor upon the normal surrounding tissues. Since the newly formed blood-vessels within the tumor are often abnormal, in that media and adventitia may not be formed, the tumor cells may penetrate the thin-walled vessels and grow along the lumen of the latter. While penetration of blood-vessels occurs usually in rapidly growing malignant tumors, it is not limited to such neoplasms. We have recently seen a marked example of this process in a slowly growing, benign fibromyoma of the uterus.

METASTASIS

The penetration of blood- and lymph-vessels by tumor cells gives rise to another striking characteristic of rapidly growing tumors, namely, the formation of secondary metastatic or daughter tumors, distant to a variable degree from the primary tumor, and quite separate and distinct from the latter. Lymphatic transport occurs more frequently in rapidly growing epithelial tumors, because these exhibit in marked fashion the invasion of tissue lymphatics by tumor cells; hence, the tumors of this type are very apt to metastasize to the regional lymph-nodes. The rapidly growing tumors originating in the supporting tissues are characterized by their richness in young, thin-walled blood-vessels; hence, such tumors spread usually by the blood stream and are prone to metastasize to the lungs. Of the abdominal organs, the liver is a frequent site of blood vascular metastasis from tumors primary in the gastro-intestinal tract. Certain tumors exhibit an especial predilection for metastasis to certain tissues; thus, tumors of the thyroid and the prostate frequently give rise to secondary tumors in the bones, and tumors primary in bone may metastasize to the thyroid. Certain tissues may be unusually resistant to the localization of transported tumor cells; the spleen is rarely the seat of metastasis, and secondary tumors are infrequent in voluntary muscle except when the latter is invaded by direct continuity. Besides the mechanical factor of transport by the blood- or lymph-vessels, local tissue resistance and chemical interrelationships between tissues and organs must be important in determining the localization of metastases.

Symmers[1] analyzed the necropsy records of 298 malignant neoplasms, 220 of which had given rise to metastases. Seventy-four per cent. of the metastasizing tumors were epithelial or mesothelial. Metastasis occurred to the following organs, in the order named: Lymph-nodes, liver, pleura and lungs, bones, and adrenals. Although the epithelial neoplasms formed secondary growths in the kidney and adrenal infrequently, sarcoma was found to be especially prone to metastasize to these organs. As the result of his study, Symmers divided the organs into: (1) Those which are frequently the seat of metastasis, but rarely of primary tumor; (2) those which are fairly often the seat of primary tumor, but rarely of metastasis;

(3) those which are rarely the seat of either primary tumor or metastasis. Armstrong and Oertel[2] attempted to determine the factors concerned in metastasis by a study of 98 cases of tumor with metastasis. They concluded that metastasis depends upon: (1) The quantity of tumor elements disseminated and the method of their dissemination; (2) the effects of injurious metabolic products of tumor cells upon the tissues, causing degeneration and inflammation, thus weakening the physiologic resistance of the tissue; (3) close embryonic relationship of tumor and tissue, tumors metastasizing more readily to organs or tissues derived from the same germ layer as that which gives rise to the primary tumor. Slye,[3] from the study of her large series of spontaneous tumors in mice, concluded that the tendency of an organ to become the seat of metastasis is transmitted by heredity.

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REGRESSIVE CHANGES

Lipoid and Hydropic Degeneration.—The cells of tumors are subject to the same degenerative changes that occur in normal tissues. In fact, because of the state into which rapidly dividing tumor cells are so prone to fall as the result of loss of physiologic regulation, they seem to react more readily than do normal cells to agencies acting from outside the cell. Fat and stainable lipoid materials may be present within the cells, especially those of epithelial tumors, in large amounts. This condition may represent, in part, a degenerative change resulting from decreased oxidation or other metabolic disturbance; in part, a heightened intracellular metabolism which leads to the storage of usable materials. Hydropic degeneration, often resulting in the formation of vacuoles in the cytoplasm, due to imbibition of fluid, occurs in edematous parts of tumors; a more or less complete lysis of cell bodies, with fading out of the chromatin staining portions of the nuclei, may result.

Mucoid Degeneration.—Mucous or mucoid degeneration at times appears to be the result of edema, at other times of the formation of true mucus. In the first case, the stroma is chiefly involved and the mucoid character of the tissue is the result of the partial solution of collagenous material in the imbibed fluid. In such tumors, the cell bodies, often with long, slender, anastomosing processes, lie widely separated in a faintly staining, gelatinous matrix, the tissue resembling that of Wharton's jelly of the umbilical cord. The tissue may give the reaction for mucin; when this reaction is absent, the term mucoid degeneration has a morphologic rather than a chemical application. Such changes occur especially in polyps of the nose, in mixed tumors of the parotid, and in cartilaginous tumors, and leads to the use of the term myxomatous. In certain epithelial tumors, the mucoid character appears to be the result of secretory activity of the tumor cells. This condition is best illustrated by certain carcinomas of the gastro-intestinal tract, particularly those of the large intestine, and by the common papillary glandular cystic tumors of the ovary. In some of the carcinomas of the colon, the condition becomes so extreme that the tumor is designated a colloid carcinoma. Large areas of tumor tissue are transformed into a gelatinous material, in the formation of which both stroma and tumor alveoli take part. The cells of the latter may be changed into swollen globular bodies filled with mucus, the nucleus forming a compressed crescent at one side. The process may lead to the actual destruction of the tumor cells, and in such tumors the small numbers of tumor cells still recognizable is often striking. The mucoid character of the stroma is due to the presence between the stroma constituents of mucus, which has escaped from the tumor cells, and to infiltration of the stroma constituents themselves by the mucinous fluid present. When such colloid carcinomas metastasize to the peritoneum, the resulting gelatinous tumor tissue may be much like that of the pseudomyxoma peritonei associated with certain benign lesions of the appendix or ovary; the differential diagnosis at times may be difficult, because of the widespread disappearance of tumor cells in the process. In the mixed tumors of the salivary glands, the myxomatous character of the stroma is likewise believed, by Böttner,[1] Schilling[2] and others who consider such tumors to be primarily epithelial in nature, to be due to imbibition of fluid secreted by the epithelial tumor cells.

Colloid and Hyalin Degeneration.—Deeply eosin-staining, glassy, homogeneous material, which has the physical characteristics of colloid, may sometimes be seen in tumors. It may occur in metastasizing thyroid tumors or in the thyroid portions of ovarian dermoids, and is then probably similar to the colloid material of the normal thyroid. In glandular tumors of the ovary and other organs, a substance of similar appearance may be present as an extracellular secretion or may occur as intracellular globules. This material is probably not chemically like the colloid of the thyroid, but derives its physical properties merely from inspissation of secreted mucoid material. Hyalin degeneration may involve either the stroma or the cells of tumors. In the former case, it is chiefly the blood-vessel walls and the collagenous connective tissue which are the seat of the change, and the process is identical with the similar one so frequently seen in tissues which are free of tumor. Intracellular hyalin transformation usually occurs in tumors derived from squamous epithelium, which normally undergoes keratohyalinization as a physiologic process. In such tumors, the change may be extreme after the action of radium. Hyalinization of stroma or of tumor cells is usually associated with slow growth of the tumor, and appears to be an expression of a defense mechanism upon the part of the body. In scirrhous carcinoma of the mammary gland, hyalin transformation may be so extreme as to lead to atrophy and disappearance of many of the tumor cells, suggesting a high degree of resistance to the original primary tumor.

Glycogenic Infiltration.—Glycogenic infiltration of tumor cells has been the subject of considerable study, because it has been thought by some to be a characteristic of tumor tissues as compared with normal tissues, and by others to be an aid in determining the origin of tumors. Best,[3] Gierke,[4] Lubarsch,[5] and others have studied the distribution of glycogen in different kinds of neoplasms. The presence of this material is not characteristic of tumor cells, as such, but of young cells with an active metabolism. It is, therefore, present in greatest amount in rapidly growing tumors, and is usually associated with intracellular fat or lipoid material; but even in such tumors, the amount may vary with the nature and origin of the neoplasm. Thus, it is usually present in largest amounts in the cells of endotheliomas, and is rarely encountered in mammary carcinomas. Lubarsch[5] has stated the following as factors which control the deposition of glycogen; origin of the tumor from embryonal cells or from cells which normally contain glycogen; absence of mucous and colloid degeneration; and the presence of fatty change. When necrosis occurs and the tumor is invaded by leukocytes, glycogen brought by the latter may be deposited.

Calcification.—As in non-neoplastic tissues, calcification may occur in tumor tissues which have undergone hyalin degeneration or necrosis, as the result of the deposition of insoluble calcium salts in dead tissue or such whose metabolism is low. In view of the great frequency of necrotic changes in rapidly growing tumors, the relative infrequency of calcification is striking, and is probably to be explained upon the basis of the inadequate circulation which causes the necrosis.

Depression Changes.—In addition to the various degenerative changes which occur in normal tissues, the cells of rapidly growing tumors frequently show intracellular changes which can not be correlated with those with which we are familiar. These alterations, which are characteristic of tumor cells, are the result of the physiologic depression and of the new regulatory mechanisms which the tumor cells utilize to overcome the depression. Nuclear chromatin, extruded into the cytoplasm, loses its basic staining properties and becomes transformed into acid staining masses. Areas of cytoplasm and daughter nuclei may die, the remaining cell body being viable and apparently capable of further reproduction when the proper nucleus-plasma relation is established by the extrusion of such dead parts of cells. In these and other ways are formed the peculiar intracellular bodies, Plimmer's bodies and so forth, which by some have been considered "cancer parasites," and which are, indeed, characteristic of tumor cells.

Necrosis.—The degenerative changes which are the result of physiologic depression occur frequently in the individual cells of rapidly growing tumors and lead to the death of a not inconsiderable number of the cells. In addition to the degenerative and necrobiotic changes which involve individual cells, the death of groups of cells or of larger areas of tumor tissue is not an uncommon occurrence in tumors. The latter process is akin to or identical with infarction, and occurs when the vessels of a tumor become obliterated or when the multiplication of the tumor parenchyma outruns the development within the tumor of blood-vessels. In the latter case, relatively large areas of tumor tissue may die, leaving only mantles of living tissue about the vessels. The tissue death is often preceded by degenerative changes, as may occur in normal tissues when the nutritive supply becomes inadequate.

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EFFECTS OF TUMORS ON THE BODY

Malignancy.—Absence of limitation of growth, rapidity of multiplication of the tumor cells, invasion, metastasis, and proneness to regressive changes are characteristic of that group of tumors to which the clinical designation, malignant, is applied. To these should be added the tendency of such tumors to recur after removal, a property dependent upon the peripheral, invasive growth of the neoplasm, which renders difficult its complete eradication. Return after removal may occur in certain tumors, which do not otherwise exhibit the usual evidences of malignancy and which histologically may be composed of well-differentiated tissue. This phenomenon is particularly well illustrated by one of the tumors of the early years of life, the recurring fibroma of the naso-pharynx. In such tumors the recurrence may be due to the fact that the matrix from which the original tumor arose may have, more or less diffusely, the property of forming tumor tissue; the new tumor would then be the result of neoplastic transformation of previously uninvolved tissue, rather than of the continuous growth of tumor tissue incompletely removed.

In addition to those characteristics of malignancy which the tumor itself shows, malignancy may manifest itself also by the deleterious effects of the tumor upon the body as a whole. Wasting and cachexia may become extreme and are associated with a secondary anemia of varying grade, even when the tumor has not led to hemorrhage. These severe general effects, as a rule, occur late; while they help to establish a clinical diagnosis, they do so at a period when diagnosis can lead to no helpful operative or therapeutic attack. Factors which may enter into the causation of these effects are the withdrawal by the rapidly growing tumor of nutritive materials necessary to the rest of the body; and intoxication by substances formed in the degeneration and necrosis of tumor tissues and by those which result from the abnormal metabolism of living tumor cells.

In addition to those harmful effects which appear to depend primarily upon the rapidity of growth of the tumor, are those which are produced mechanically, often by neoplasms not otherwise malignant. Benign tumors of the gastro-intestinal tract may interfere mechanically with nutrition or may lead to obstruction. Tumors of the brain may injure chiefly through their pressure effects. Some of the benign neoplasms of the intestine and urinary bladder in children have caused severe anemia or death by hemorrhage.

Abnormal Development Due to Tumors.—Those general disturbances which are the result of the malignancy of tumors are no different in children than in adults. Certain tumors of childhood, however, since they occur in the developmental period of life, are associated with striking general abnormalities which have led to much discussion. In brief, these abnormalities consist of excessively rapid somatic growth and precocious sexual maturity. It is especially tumors of the gonads, the adrenal, and the pineal body which are associated with this symptom complex. For a relatively small number of cases, the involvement of one or another of these organs has been established anatomically by necropsy or by operation. Upon the basis of these fairly well-established cases, a large number of others is recorded clinically in the literature, but without the anatomical evidence which warrants utilization of the material. Reviews of the literature dealing with sexual precocity in relation to tumors have been given by Leiner,[1] by Tierney,[2] and by Reuben and Manning;[3] and for the individual organs which may be involved, there have been valuable studies by others. In the discussion which follows, only those readily accessible cases which have an anatomical basis will be considered.

Tumors of the Ovary.—Of organs whose involvement has been associated with the abnormality under discussion, the ovary and the testis deserve consideration because they might, *a priori*, be expected to have such influences upon somatic and sexual development. The number of recorded cases is, however, small.

Neurath[4] refers to three cases of ovarian tumor in young girls, Geinitz, Riedl, and Meurer each having reported one, associated with enlargement of the uterus and premature development. In the Geinitz case, which was published in 1862, menstruation was said to have begun at the age of 19 months. Death occurred at 21 months, the breasts and pubic hair at this time being like those of an adult woman. The tumor was called a sarcoma of the ovary. Riedl's[5] case was aged six years. She had menstruated since four years of age. The mammæ were well developed and each had a prominent nipple and areola. Pubic hirsutes was present, the labia were prominent, the vagina was large, and the uterus was the size of that of a girl aged 17 or 18 years. Menstruation ceased after removal of the tumor, which was a round-cell sarcoma of the left ovary. Glynn,[6] in 1912, mentioned a similar case of Parkes Weber and three cases of Hoffacker.

In Lucas'[7] case, a girl of seven years, menstruation had been established, the mammæ were enlarged, and pubic hair was present; a tumor of the ovary, described as an alveolar round-cell sarcoma, was removed, recovery from the operation being followed by cessation of menstruation and decrease in the size of the breasts. In Gaudier's[8] case, a girl of four years, in whom menstruation had been established and whose breasts were enlarged, there was a tumor of the ovary resembling a hypernephroma. Debeyre and Riche[9] have also reported a hypernephroma of the ovary, associated with hypertrophy of the external genitalia and the mammæ and with the presence of pubic hirsutes. The child was four years old. The hypernephroma of the right ovary reported by Downes and Knox[10] occurred in a girl aged 3½ years. The vulva was enlarged and there was a slight growth of pubic hair; no mention was made of menstruation and in other respects also the case does not appear to have been a quite typical one. The case of Brohl (in Glynn[6]) may be included, although not a true tumor of the ovary. The child was seven years old, she had menstruated, and was physically developed beyond her years; removal of a large cyst of the ovary was followed by cessation of menstruation. A case reported by Lenz,[11] in 1913, was 11 years old at the time of observation (Fig. 270). Menstruation had begun at the age of five years and was irregular. At seven years the mammæ enlarged and the pubes became covered with hair. A tumor of the ovary, termed a cystosarcoma, was removed at 11 years. Lenz gave a thorough discussion of sexual precocity and tabulated 130 cases from the literature dating back to 1658. In only five of this series, including Lenz' own, was the nature of the tumor established by necropsy or operation. One was a tumor of the adrenal included below, two were the tumors of the ovary reported by Geinitz and Riedl and noted above, and one was a sarcoma of the ovary recorded by Revern in 1802. Revern's patient was 3½ years old at the time of death. The breasts and pubic hirsutes were like those of an adult woman, the pelvis was broad, and there was generalized hypertrichosis; no mention is made as to whether menstruation had been established. Knewitz[12] reported an adenocarcinoma of the ovary in a girl aged five years, who had menstruated for the first time when two years old. When 4¾ years old she began to grow rapidly and the breasts became "markedly enlarged." Siegel[13] reported a case of cystic sarcoma of the ovary in a girl aged eight years. The clinical data are incomplete, but the mammæ were abnormally large for the age and there was a heavy growth of hair on the external genitalia, which were larger than normal. Verebély[14] reported the case of a girl aged six years, who had begun to menstruate one year previously. She was 10 cm.

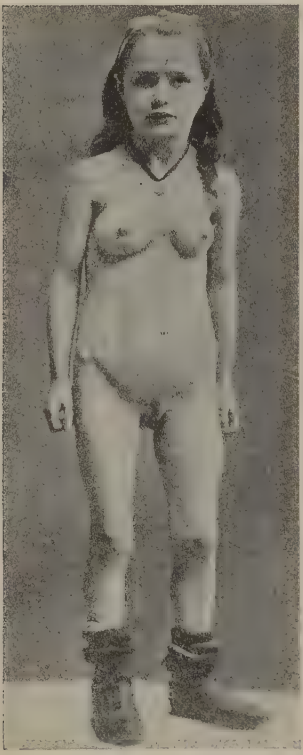

Fig. 270.—Precocious development associated with sarcoma of the ovary in a girl aged 11 years. (Lenz.[11])

taller than the average for her age. The breasts were enlarged, axillary and pubic hirsutes were present, the labia were large and pigmented, the vagina was wide, and the uterus was as large as that of a woman aged 18 years. Removal of a large sarcoma of the ovary was followed by loss of hirsutes, cessation of menstruation, and decrease in the size of the breasts. Harris[15] has reported a solid ovarian teratoma with carcinomatous areas, in a girl aged five years and ten months. She had begun to menstruate at five years, the breasts were large, and axillary and pubic hair was well developed. In 21 examples of teratomatous ovarian tumors in girls under 14 years of age tabulated by Harris, there was only one other case, credited to Fusino, in which this type of tumor was associated with premature development; this child was five years old. Reuben and Manning[3] record a carcinoma of the ovary in a girl of 7½ years; she had grown more rapidly than normal, the breasts were large, pubic hair was present, but menstruation had not been established.

In the above cases of ovarian tumor, menstruation occured at such an early age that it may be considered truly precocious. Steffen's[16] tabulation of 10 malignant ovarian tumors includes one case in which menstruation was established at 11 years and two at 13 years. Summarizing the cases noted above, we find 19 cases of tumor of the ovary (exclusive of the three of Steffen) and one of cyst, in which the abnormality of development consisted of premature growth of pubic hair, early menstruation, mammary development, and moderate increase of body size. Three of the ovarian tumors were hypernephromas.

Tumors of the Testis.—Small as the above group of cases is, it outnumbers those in which a tumor of the testis has been associated with precocity. Sacchi[17] has reported a case of enlargement of the left testis, with puberty at five years of age. At nine years the boy was 5 ft. 6 in. tall, he weighed 97 lb., had a black beard and heavy pubic hair, and was fully developed sexually. Following removal of the tumor, which was termed an alevolar carcinoma, the beard disappeared, but the growth of the hair on the upper lip and on the pubes was still heavy; the remaining testis and the penis decreased in size. This is apparently the only recorded example of tumor of the testis associated with precocious development.

Adrenal Tumors.—Cases of tumor of the adrenal with abnormal development are more numerous. Glynn[6] has tabulated 17 cases, three of which were males, the rest females. Of this group of cases, that of Adams, Raymond and Johnson was the oldest. This was a boy of 16, who had had symptoms since the age of 10 years. The hair of the pubes and beard was well developed, and the external genitalia were large. The tumor was a hypernephroma of the adrenal, with liver metastases. In the remaining cases, the age at death varied from 1 year and 2 months to 11 years, and symptoms had been present for a few months to as long as 5½ years. Since most of the tumors formed metastases, it is necessary to conclude that in those cases with longer duration, the malignancy of the tumor was a terminal development. In the females, the manifestations, in general, consisted of abnormally rapid and excessive body growth, excessive growth of hair, adiposity, and enlargement of the mammæ and of the external genitalia. The internal genitalia, as a rule, were small and infantile.

Of the two male cases included by Glynn[6], in addition to the one mentioned above, one, reported by Linser, was five years old at the time of death. Symptoms had been present since the age of 1¼ year. Pubic hair was present, the genitalia were large, he was sexually active, and the weight and development were those of a boy of 15 years. The other male case, reported by Guthrie and Emery, died at 4¾ years, symptoms having been present since the second year of life. Hair was present on the face and pubes, he was "enormously fat," but the genitalia were not unduly developed. He was mentally precocious. Additional cases of adrenal tumor in males with precocious sexual development have been reported by Baldwin[18] and Tschernobrow.[19] In Baldwin's case the age at death was five years. At 18 months of age the penis began to enlarge and reached the size of that of an adult; the facial appearance was that of a middle aged man; the testes were small. The tumor was a hypernephroma of the left adrenal, with metastases. Tschernobrow's case was a boy aged 11 years, in whom progressive hirsutes began at the age of three years. The tumor was a hypernephroma of the right adrenal, with metastases.

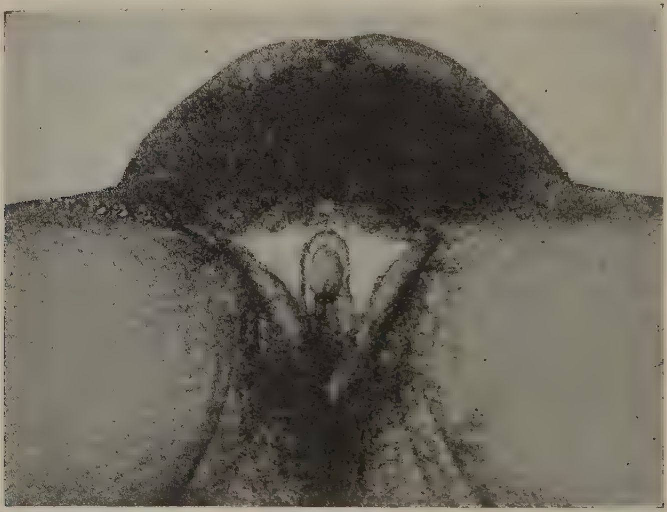

Fig. 271.—Hypertrophy of the external genitalia and pubic hirsutes associated with hypernephroma of the adrenal in a girl aged 7 years. (Jump, Beates and Babcock.[20])

Since Glynn's publication, additional cases in girls have been reported by Jump, Beates and Babcock [20] Mathias,[21] van den Bergh,[22] Schiff,[23] Ambrozic and Baar[24] Hoag,[25] Collett,[26] Fraenkel,[27] Scabell, [28] Siegel,[13] Gibbon,[29] Schmidt,[30] and Sachs,[31] the last five having been reported within the present year (1924).

The case of Jump, Beates and Babcock[20] was a girl aged seven years, who began to grow rapidly when one year old. At this early age hair developed in the axillæ and on the pubes, and later on the legs and back. Rapid body growth was associated with striking mental and physical development. At seven years she was like a boy of 17 or 18 years. She had never menstruated. The labia and clitoris were markedly developed (Fig. 271), but the internal genitalia were of the normal, infantile size. The breasts were not enlarged and were of the masculine type. The tumor was a hypernephroma of the right adrenal. Mathias'[21] case died at the age of 18 years. Since three years of age she had had a beard and a heavy growth of hair on the body, and has been considered an example of masculine pseudohermaphroditism. At nine years she had reached her final height of 4 ft. A tumor of the adrenal had been diagnosed. During the final year of life this began to grow rapidly and was removed. The tumor was an adrenal hypernephroma. Van den Bergh's[22] case was a girl aged three years, who was 5 in. taller than normal and had an adult aspect, especially as regards the external genitalia. At necropsy a hypernephroma of the left adrenal was found. Schiff's[23] case was a girl aged two years. Adiposity and heaviness of the voice had been present for 2½ months. Pubic hair was well developed, and hair was present on the chin. The breasts and genitalia were normal.. The tumor was a hypernephroma of the right adrenal, without metastases. Ambrozic and Baar's[24] case was a girl aged three years, who since one year of age had had a heavy voice, had grown rapidly, and was mentally precocious. The external genitalia were large, and the pubes were covered with hair. The breasts were small. The internal genitalia were normal. The tumor was a hypernephroma of the left adrenal, with metastases in the lungs and brain. Hoag's[25] case was a girl aged four years and three months. The external genitalia were of adult size and were sparsely covered by hair 3 cm. long. The internal genitalia were of the infantile type. The tumor was a hypernephroma of the right adrenal, with metastases in the lungs.

Collett's[26] case was a girl aged 18 months when first seen, in whom the growth of pubic hair began at from six to eight months of age. This was followed by hirsutes of the trunk and extremities, coarsening of the voice, and obesity. The clitoris was enlarged and the external labia were prominent. Menstruation had not been established. The internal genitalia were small. At operation, a year after the first admission, a cortical hypernephroma of the right adrenal, measuring .35 by 2.5 by 2.2 cm. was removed. Two years after the operation the child's condition was greatly improved; the hirsutes had disappeared except for a few hairs on the labia, the latter were less prominent, the clitoris had not increased in size, but the voice was still deep. The case reported by Fraenkel[27] was a girl aged nine years. There was a heavy growth of hair on the body and face, and the vulva and clitoris were hypertrophied. The tumor was a hypernephroma of the right adrenal.

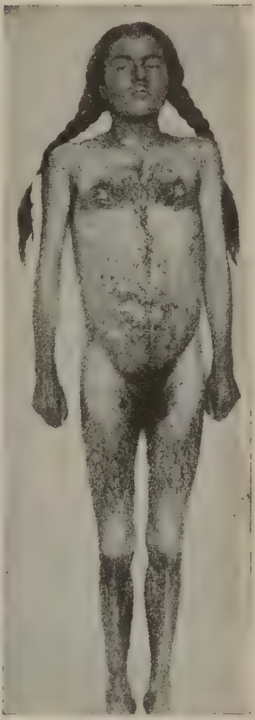

Fig. 272.—Virilism and hypertrichosis associated with hypernephroma of the adrenal in a girl aged 15 years. (Scabell.[28])

Scabell's[28] case was a girl aged 15 years. At 12 years of age she increased in height and strength, and by the end of the thirteenth year the entire body was covered with hair. The voice became deep and masculine. Menstruation began at 14 years, but was scanty and occurred only a few times. The body form was masculine, with narrow hips and relatively broad shoulders; the mammæ were not developed (Fig. 272). The external genitalia were like those of an adult woman; the clitoris was 3.5 cm. long. Laparotomy revealed an inoperable hypernephroma of the left adrenal. The ovaries were small and atrophic, and the uterus was infantile. Siegel's[13] case was a child aged three years, who was admitted in uremic convulsions due to acute nephritis. She was large for her age, and there was an excessively heavy growth of hair on the head. Pubic hirsutes was present and the external genitalia were abnormally large. The tumor, which had completely replaced the right adrenal, was called a sarcoma of the cortex. The internal genitalia were not increased in size. Gibbon's[29] case was three years old. Four months before coming under observation the abdomen began to enlarge, and hair appeared in the axillæ and on the pubes, labia and back. The clitoris was greatly hypertrophied. The uterus and ovaries were infantile, and menstruation had not occurred. A hypernephroma of the left adrenal, 13 cm. in diameter and weighing 720 gm., was removed. Schmidt's[30] case was nine years old. At eight years of age the child was unusually strong, but not oversized. Five months before coming under observation hair appeared on the lip and chin, requiring shaving twice weekly. Pubic hirsutes appeared and was of the male type; the voice became deep. The breasts were of the masculine type. The clitoris and labia were large. The left adrenal contained a walnut-sized adenoma, and the right adrenal had been transformed into a large hypernephroma. The internal genitalia were atrophic. Sachs'[31] case was aged 3¼ years. The parents had noticed within a few days after birth that the genitalia were abnormally large, and as the child grew the condition was believed to be one of pseudohermaphroditism. At three months of age pubic hair appeared. At the time of admission she was somewhat taller than normal, the body proportions were normal, and there was no obesity. Hirsutes was present on the body, being heaviest on the back. The external genitalia were like those of an adult woman and were covered with a heavy growth of hair. The clitoris was 2.5 cm. long and looked like a penis, with a well-formed glans, prepuce and frenum. The child had not menstruated. Death occurred during the operation for removal of a hypernephroma of the left adrenal. The internal genitalia were slightly enlarged.

In the adrenal tumors of girls, the developmental anomaly, when present, involves the secondary sexual characters more markedly than the primary, and is of the nature of a masculinization rather than a true precocious development of sexual activity. However, in some of the cases, menstruation was established at an early age and the mammæ were unusually developed. In one of the male cases, the genitalia were not excessively large, but in the others enlargement of the genitalia was associated with sexual activity. Feminization of the male as the result of adrenal tumor is apparently rare; Mathias[21] reported such a case in a male aged 26 years, who died of an adrenal hypernephroma. In a few of the cases there was moderate pigmentation of the skin, but not of such a grade as occurs in Addison's disease. Some of the tumors have been described as alveolar sarcoma and one or two as carcinoma. Glynn[6] believed that all were hypernephromas of the adrenal cortex and that there was no authoritative case of association of developmental anomaly with adrenal tumors of other types. Most of the cases were mentally dull, although a few were mentally as well as physically precocious.

Tumors of the Pineal Body.—Whereas most of the cases of gonadal and adrenal tumor with precocious development have occurred in girls, tumors of the pineal body with similar association have, with one exception, been in boys.

Bailey and Jelliffe[32] tabulated the pineal tumors reported previous to 1911, and Horrax[33] has made a complete tabulation to 1916. These authors, as well as those others who have written upon the subject, include the five classical cases of pineal tumor with sexual precocity which are referred to in all of the collective papers. These are the cases of Gutzeit[34] (1896), aged 7¾ years; of Ogle[35] (1899), aged six years; of Oestreich and Slawyk[36] (1899), aged four years; of Frankl-Hochwart[37] (1909), aged 5½ years; and of Raymond and Claude[38] (1910), aged 10 years. All of these were boys. In all, the height was excessive for the age, pubic hair was well developed, and enlargement of the penis was striking. The testes, however, were small. Raymond and Claude's case is described as being fat; the weight was 39 kg. for a boy of 10 years; Frankl-Hochwart's case was markedly fat; and in Oestreich and Slawyk's case the mammæ were large and colostrum could be expressed; but the tendency to extreme adiposity does not appear to have been a striking feature in these cases. In the cases of Gutzeit, Ogle, and Frankl-Hochwart, the tumor was a teratoma. In Oestreich and Slawyk's case it was called a cystic psammosarcoma; Askanazy,[39] from whose laboratory this case was reported, later considered the tumor a teratoma. The tumor in Raymond and Claude's case was termed a glioma. In addition to the above five classical cases, mentioned by everyone who has written upon the subject, the following cases have been reported: Horrax[33] has reported the case of a boy aged 12 years, in whom rapid mental and physical development occurred. He was 5 ft. 3 in. tall at the age of 12 years, and the genitalia were overdeveloped (Fig. 273). There was no adiposity. The tumor was diagnosed a struma of the pineal by Councilman. Lereboullet[40] also described a case of pineal tumor in a 12 year old boy, whose growth was rapid up to the age of nine years. Growth then proceeded more slowly, but genitalia, hirsutes and voice rapidly developed until they were like those of an adult. The tumor was termed a neuroepithelial glioma. Bailey and Jelliffe's[32] case, a boy also aged 12 years, had been bright and normal up to the age of 10 years. He then became markedly fat. There was no pubic hair, and the genitalia were not abnormal. The tumor was a teratoma of the pineal gland. Marburg's[41] case is the only one of the pineal group in a female. One year after the onset of the first symptoms she became very fat; at the age of nine years she weighed 29.3 kg. and was 123 cm. high. The tumor was a mixed tumor. Bailey and Jelliffe's case and that of Marburg are alike in that adiposity was the striking feature, genital overdevelopment being absent; in these features, these cases suggest the syndrome which has been ascribed to pituitary involvement.

The accessible literature contains 20 cases of gonadal involvement with the symptom complex under discussion, 32 cases of adrenal tumor, and nine of pineal body involvement. The sex of the patients in the three groups was as follows: Gonadal group, 19 females and one male; adrenal group, 27 females and five males; pineal group, eight males and one female. In the gonadal and adrenal cases, the preponderance of females over males is as striking as is that of males over females in the pineal body tumors.

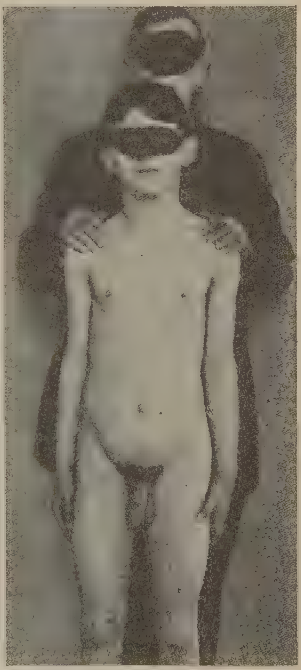

FIG. 273.—Precocious development associated with tumor of the pineal in a boy aged 12 years; height 5 ft. 3 in. (Horrax.[33])

Pathogenesis of Precocious Development.—The explanation of the relation of the tumor to the general condition produced has led to much speculation, and, in view of the lack of exact knowledge of disturbances due to supposed endocrine abnormality, must continue to remain speculative and theoretical. It is a simple matter to state that hyperplasia of an endocrine organ leads to hyperfunction, and that increased physiologic activity manifests itself by the described general abnormality of development. But biologic proof that morphologic evidence of increase in the number of specific cells of a given endocrine structure means increased functional activity is difficult to adduce.

In Gonadal Tumors.—That the gonads have a direct influence upon somatic and sexual development appears well established, although the part which the specific germ cells and the so-called interstitial cells have in this process is less clear. Upon the supposition that a gonadal tumor might lead to an increased formation of the kind of tissue which influences development or, through stimulation, might increase the activity of the normal tissue present which has this influence, it is easy to conclude that the developmental changes associated with gonadal tumors are simply the expression of a true precocious puberty. Klemperer,[42] who accepted the hypothesis that the interstitial cells of the gonads are essential for the development of normal sexual characteristics, believed that the tumors of the ovary and the single tumor of the testis associated with sexual precocity were sarcomas derived from the interstitial cells. If his interpretation of these tumors can be accepted and if the rôle of the interstitial gonadal cells is granted, then hyperactivity of tumor tissue with specific properties might be adduced as the cause of the developmental anomalies noted.

In Adrenal Tumors.—In the case of the adrenal tumors, a hypothetic explanation is more difficult. Furthermore, the resulting general condition does not appear to be a true precocious puberty, in that the secondary sexual characters are concerned to a greater degree than the primary ones, and the changes in the former are not such as are normal for the sex. Interesting in this connection is the apparent relation of adrenal cortical hyperplasia to genital abnormalities in young adults and to pseudohermaphroditism. Glynn[6] has tabulated six examples of adrenal hyperplasia in young adult females, associated with changes in the sex characters, and 13 examples of pseudohermaphroditism, chiefly feminine, in which there was bilateral adrenal hyperplasia or the presence of accessory misplaced adrenal rests. Adrenal tumor and hyperplasia are associated with abnormalities in sexual characteristics more frequently than are neoplasms of the gonads or pineal body. Apparently we must ascribe to the adrenal some morphogenetic activity, greater in the female than in the male; but the exact mechanism by which the effect is produced has not been determined.

That there is a closer relation between the adrenal cortex and the gonadal system in the female than in the male, has recently been shown by Jaffé and Marine,[43] who found a definite enlargement of the ovaries of rabbits which survive double adrenalectomy. The increase in the size of the ovary as a whole is due to hypertrophy of the interstitial cells. In male rabbits, the same procedure caused no changes in the testes. Perhaps these experimental observations may give a clue to the greater frequency of abnormal development in girls with adrenal tumors, as compared with boys with similar tumors. Krabbe[44] has claimed, in agreement with others, that the medullary portion of the ovary, in its early development, is composed of testicular tissue derived from the anlage of the adrenal cortex. An excessive amount of adrenal cortical tissue is held by him, therefore, to subject the developing female organism to the action of an increased amount of hormone with testicular activity, resulting in masculinization. In the male, such excessive activity would merely cause premature sexual development along normal male lines. Schmidt[30] accepts the doctrine, for which cytologic research of recent years offers much support, that sex is predetermined at the time of fertilization. In the cases of true and pseudohermaphroditic anomalies associated with adrenal hyperplasia, he holds that both the genital and the adrenal condition are independent developmental anomalies. In the cases of adrenal tumor associated with genital anomalies and precocity, he concludes that the heterosexuality, if present, is the result of developmental anomaly, but the precocity is the effect of the tumor. Since in those cases where the condition of the ovaries has been mentioned the latter were atrophic, the element of precocious development of secondary sexual characters might be the result of loss of ovarian function or of the action of material produced by the adrenal tumor.

In addition to the association of tumors of the gonads and adrenal with the sexual maldevelopments of the precocious types discussed above, and of hermaphroditism with hyperplasia of the adrenal cortex, a frequent combination of hermaphroditism with tumors of the gonads has been noted by Pick,[45] who collected 31 cases of hermaphroditism with gonadal tumors. Whether the striking frequency of such associations is proof that the gonadal condition is the primary factor in the causation of the genital abnormalities, as Pick maintained, or that both the hyperplastic or neoplastic lesions of the adrenal or gonads and the genital anomalies are the result of the same developmental error, as held by Schmidt, can not be determined. Because of the close embryologic origin of the adrenal and the gonads, the former may have some of the morphogenetic properties which are more characteristic of the latter and may act directly upon the body as a whole. Or the adrenals may unfold their activity through the intermediation of the gonads, the adrenal acting first upon the ovary chemically or by means of a hormone. The adrenal tumors which have been associated with somatic abnormality have usually been hypernephromas of cortical origin; the statement has been made that sarcoma or the more frequent neuroblastoma, occurring in childhood, is not associated with the precocity complex. This would make it appear that any morphogenetic action which the adrenal may have resides in the cortical rather than in the medullary tissue. In this connection, it is interesting to note that pigmentation of the skin has been infrequent in the adrenal cortical tumors of children. Also interesting, is the fact that the ovarian tumors in the cases of Gaudier,[8] Deheyre and Riche,[9] and Downes and Knox[10] were hypernephromas.

In Pineal Tumors.—In the pineal tumors, an explanation of the recorded facts is as difficult as in the adrenal neoplasms. The association of pineal tumor with sexual precocity and abnormal development early led to the hypothesis that the pineal body, which atrophies at about the age of puberty, has some influence upon somatic development before this time. If we grant such an influence in the case of the normal pineal, it would seem necessary to suppose that the presence of pineal tissue acts upon the gonadal system and restrains that activity of the latter which, at puberty, manifests itself in the development of characters associated with sex. Such a protective or inhibitory function against premature activity of the gonads, was, in fact, postulated by Neurath[4] as a normal function of both the pineal body and the adrenal cortex. If this is the mode of action, then the necessary corollary is that a tumor of the pineal body exerts its effects through premature destruction of the gland, rather than through hyperaction. Unfortunately for this apparently satisfactory hypothesis, experimental evidence is contradictory. Horrax,[33] it is true, claimed to show that extirpation of the pineal body in young male guinea pigs was followed by hastened development of the sexual organs, as indicated by their size and by microscopic evidence of active spermatogenesis.

If absence of pineal activity, through destruction by tumor, is the factor which leads to precocious development, then it is difficult to correlate a case reported by Zandren,[46] either with the clinical evidence furnished by tumors or with the experimental results of Horrax. In Zandren's case, a boy who died at the age of 16½ years, development had been normal until the tenth year, but was retarded from this time on, resulting in a condition of marked infantilism. At autopsy the pineal body was found to be absent. Zandren, as a result of this case, claimed that the function of the pineal body is the initiation of puberty rather than its inhibition. Such a view would necessitate a belief in the hyperactivity of the pineal in those tumors which have been associated with precocity, which is contrary to the destructive character of such tumors or to the supposed disappearance of the normal pineal before the establishment of puberty. It is to be noted that not every tumor of the pineal body developing during the early period of life has been associated with abnormal development, and the same is true of gonadal and adrenal tumors. Marburg,[41] in 1913, tabulated 54 cases of pineal tumor at all ages, of which 11 occurred at ages up to 10 years, and 16 at ages 10 to 20 years; of these, only the five cases mentioned above as classical were associated with precocity. Bailey and Jelliffe's[32] tabulation of 60 pineal tumors includes 21 at or before 16 years of age; in only eight of these was precocity present.

Growth Hormones of Embryonic Tissues.—That an association exists, in a certain proportion of cases of tumors of the gonads, adrenal and pineal body, between the tumor and the complex under consideration, cannot be doubted. This association has led to the belief in supposed specific activities of the organs named in relation to growth and sexual maturity. Askanazy[47] has proposed an explanation which denies a specific relation of certain organs to the general condition. He believed that the reported pineal tumors which were associated with abnormal development were all teratomas. In the older literature he found a few cases of tumors of organs other than the gonads, adrenal or pineal body, which were associated with a similar complex. These tumors were also teratomas or choriomas. He, therefore, concluded that the precocious development is due to a hormone produced by the embryonic tissues of teratomas, basing his belief upon the theory that the tissues of the normally developing embryo furnish their own growth stimuli. He was forced to admit that most teratoid tumors do not lead to abnormal body development, and, therefore, took refuge in the statement that not every teratoid embryonic tissue has the property of liberating a growth stimulating hormone. A most important objection to Askanazy's view is the fact that adrenal cortical tumors, which have none of the characteristics of teratomas, are associated with developmental anomalies more frequently than are the teratomatous tumors of the pineal body.

Tumors of the Hypophysis.—The striking feature of the several groups of tumors discussed above is the element of sexual precocity. In the adrenal cortical neoplasms, as already pointed out, this element appears to be less sharply marked, and the genital involvement approaches sexual inversion more nearly than precocity. Tumors of the hypophysis may show a still further gradation, in that the element of sexual precocity may be entirely wanting, such involvement of the genital system as occurs being one of arrest of development rather than overdevelopment. But because certain tumors of the hypophysis may be associated with somatic developmental anomalies, this association may be briefly discussed at this point, although it is to be noted that these abnormalities are not limited so sharply to the period of childhood as is the case with the other tumors considered.

Fröhlich's Syndrome.—Tumors which destroy the hypophysis may be associated with the Fröhlich syndrome of obesity and hypogenitalism. Scanty growth of hair, diabetes insipidus, and, in the male, the female type of pelvis and enlargement of the mammæ have been described. The tendency to obesity, which has been noted also in some of the pineal and adrenal tumors of children, is usually more marked in the pituitary tumors and may occur at any period of life. It is, perhaps, a metabolic rather than a developmental disturbance. Strada,[48] who reported a squamous cell epithelioma of the craniopharyngeal duct in a markedly corpulent 19 year old girl, tabulated from the German literature 33 cases of pituitary tumor associated with obesity. Of this group, only five, including Strada's case, occurred in individuals up to the nineteenth year of age. Pechkranz' case was a 17 year old boy, with a small penis, overdeveloped mammæ, and no body hirsutes; the tumor was a vascular sarcoma. In Babinski's case of epitheliomatous duct tumor, menstruation had not been established up to the seventeenth year of age and the genitalia were infantile. Erdheim's[49] case was also an epithelioma of the duct, in a boy of 16 years; the entire genital system was underdeveloped and there was little hair on the body. Bregmann and Steinhaus[50] reported a cyst of the duct in a seven year old girl, in whom adiposity had been of a year's duration.

Destruction of the hypophysis, with a loss of its specific endocrine activity, has been proposed as an explanation of the changes noted. Erdheim,[49] however, has supposed that the effect is due to pressure by the pituitary tumor on centers located at the base of the brain, and not to involvement of this organ itself. Here again we have to note that not all hypophyseal tumors are associated with the described and supposedly characteristic developmental or metabolic abnormality. In connection with the question of the relation of as yet not localized centers in the mid-brain to such anomalies as are usually ascribed to disturbance of the specific activities of the pineal and hypophysis, it may be noted that the most recently reported case of typical precocity syndrome was associated with a gliomatous and neurofibromatous tumor of the base of the brain which did not involve either pineal or hypophysis. This case, reported by Schmalz,[51] occurred in a boy aged 12 years, whose sexual and somatic development were like those of an adult.

Gigantism and Acromegaly.—In other pituitary tumors, gigantism of the acromegalic type has been observed. This manifestation usually does not make its appearance in the early period of life, but Brissaud and Meige[52] claimed that gigantism arising during childhood might become transformed into acromegaly in later life. PaténYi[53] found the anterior lobe of the hypophysis enlarged in a 10 year old acromegalic boy. Development of the genital system is not proportional to the somatic overdevelopment, and sexual precocity is not the striking feature in early acromegaly that it is in the pineal tumors. On the contrary, there may be the same loss of sexual function and the same condition of hypogenitalism that occur in some of the destructive pituitary tumors with obesity. When the hypophysis is involved in acromegaly, the tumor is usually adenomatous in character. This has led to the belief that hyperfunction upon the part of the glandular portion of the pituitary is responsible for the acromegalic syndrome.

Relation of Hypophysis to Fröhlich's Syndrome and Acromegaly.—The absence of either the Fröhlich syndrome or acromegaly in a considerable proportion of tumors of the hypophysis; the occurrence of either of these complexes, which differ so widely from each other, with tumor of the same region; the association of hypogenitalism with both obesity and acromegaly, present a variety of possibilities which make difficult an accurate evaluation of the general effects of pituitary tumors and which have led to widely divergent views of the relation of tumor to the observed conditions. The typical Fröhlich syndrome has been present in cases in which tumor of the hypophysis was excluded with absolute certainty by careful anatomical examination. In such cases there have been cranial tumors situated elsewhere than in the hypophysis, most often in the base of the brain, or even non-neoplastic lesions which have led to dilatation of the third ventricle. Such facts have seemed to offer strong support to the view that the obesity-hypogenitalism complex is due to pressure upon centers located at the base of the brain and not in the pituitary itself. Those who would make the latter structure solely responsible meet the objections raised by such observations as the above by the statement that other cranial tumors and particularly hydrocephalus exert their effects by pressure on or destruction of the posterior lobe of the hypophysis. Furthermore, in those cases in which a hypophyseal tumor has actually been present but without the Fröhlich syndrome, it has been claimed that such tumors have failed to destroy the posterior lobe or to bring about hypofunction of this lobe.

Those who deny a relationship between hypophysis and acromegaly find their strongest arguments in cases of pituitary tumor without acromegaly on the one hand, and cases of acromegaly without hypophyseal tumor or tumor of any kind on the other hand. The defenders of the pituitary theory of acromegaly meet the objections raised with the statement that not every tumor of the hypophysis does or should cause acromegaly, because the latter condition can be due to only one specific type of tumor, namely, an adenoma of the anterior lobe; the supposed small round-cell sarcomas which have been associated with acromegaly are, therefore, held to be derived from the anterior lobe acinar cells. The argument that there has been no involvement of the hypophysis in a certain percentage of cases of acromegaly is met by the statement that these have not been true cases of acromegaly. The strongest proponent, among pathologists, of a specific relation between hypophysis and acromegaly is Bernhard Fischer,[54] who goes so far as to say, very emphatically, that no case of true acromegaly has ever been reported which did not show the adenomatous type of tumor of the anterior lobe of the hypophysis ("Ich . . . behaupte . . . das . . . ein absolut einwandsfreier Fall von Akromegalie ohne die typischen Hypophysisveränderungen noch nicht publiziert ist"). For this author the obesity syndrome is due to destruction or hypofunction of the posterior lobe of the hypophysis, acromegaly to hyperplasia, adenoma or carcinoma of the anterior lobe with hyperfunction. The hypogenitalism, which may be part of either syndrome, is held to be due to involvement of the posterior lobe itself in Fröhlich's syndrome, or to pressure upon the posterior lobe by the adenomatous tumor of the anterior lobe in acromegaly.

Rössle,[55] in a recent critical review of the abnormalities of growth, has made the criticism that the evidence furnished by those tumors which are associated with developmental anomalies is incomplete, in that careful examination of the growth centers of the skeleton has usually not been made. Individuals with such tumors usually die before the period of growth is completed, so that it has been impossible to determine whether true excessive growth might have occurred. In a few of the tumor cases it has been noted that growth, although rapid for a time and precocious, ceased before the individual reached an excessive height. Rössle claims that the somatic developmental anomaly in the tumor cases is a compression of the growth period of youth into a shorter range of time than normal, rather than a true overgrowth. He believes that the primary factor is an abnormally early sexual ripening, whether due to the tumor or to other causes is immaterial, and that it is the sexual precocity and not tumor which furnishes the somatic growth stimulus.

The true explanation of the interesting conditions which have been discussed is a matter for future research. Speculations based upon specific hyperfunction in gonadal tumors; upon hyperfunction or hypofunction in adrenal, pineal and hypophyseal tumors; upon interrelationships within an endocrine system, one organ of which may be the seat of tumor; or upon hormones liberated by teratoid embryonic tissues, are interesting but at present unproved hypotheses.

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THE CHEMISTRY OF TUMORS

The chemical investigation of tumors has dealt with alterations in the general metabolism and with the chemical composition of tumors themselves.

Metabolism in Neoplasia.—Metabolic studies have had for their aim the detection of abnormalities which might be ascribed directly to the tumor itself. That a mass of neoplastic tissue, independent of control by the rest of the body, should give rise to chemical products different from those produced by the normal tissues, would appear to be almost selfevident. However, scientific proof of such an altered chemism is difficult to furnish, and satisfactory evidence upon this point acceptable by all has not been adduced. Perhaps this is because the abnormal products which may be produced by tumors are present in such relatively small amounts in any given period of time, as compared with the products of the normal tissues, that our present methods fail to detect them.

Much attention has been given to the study of metabolism in the attempt to discover alterations which might explain the cachexia which is so striking in the later state of many malignant tumors. F. Müller[1] and other earlier observers claimed that nitrogen excretion is increased in individuals with tumors. This earlier work was based chiefly upon the study of cases with gastro-intestinal carcinoma, in whom cachexia was marked. A just criticism is that in such cases the increased nitrogen excretion is the result of digestive disturbances, starvation, and especially of the cachexia itself, rather than the expression of some process which is specific for tumor and which causes the cachexia. Study of cases without cachexia has failed, as a rule, to detect any variations from the normal. Glossser and Frisbie,[2] in a study of four cases of carcinoma (one each of the esophagus, pylorus, kidney and vulva) and one case of sarcoma (of the skin and subcutaneous tissue), found that the patients, who were all in the terminal stage of their disease, were in nitrogenous equilibrium or showed a negative balance no greater than that of the normal control on partial protein starvation. Further work, by Braunstein,[3] Lewin[4] and others, on cachectic individuals with tumors situated elsewhere than in the gastro-intestinal tract, has often confirmed the earlier findings of increased nitrogen excretion, but has not furnished incontrovertible proof that this phenomenon is due to increased destruction of body protein brought about by tumor derivatives. The problem is complicated by a number of factors, such as fever, necrosis of tissue, leukocytic infiltration, etc., which of themselves, when not associated with tumor, may lead to a negative nitrogen balance.

In neoplasia, increased destruction of protein may be the important factor; but the increased nitrogen output may come from tumor tissue which is undergoing destruction, rather than from body protein broken down under the influence of the tumor. That the destruction of tumor tissue is an important factor in the clinical condition of the host is indicated by Brown and Pearce's[5] recent study of a transplantable rabbit carcinoma, in which it was found that the animals appeared well and increased in weight until regressive changes in the tumor began, when loss of weight, which was often rapid and marked, might occur. Among the earlier investigators, v. Moraczewski[6] found a decreased elimination of nitrogen, rather than the increase described by others. This positive balance he ascribed to an increased demand for nitrogen by the tumor tissue. This older belief, that the nutritive demands of tumors might manifest themselves in general chemical changes, appears again in the work of some recent investigators, who have studied the alterations in the blood.

Wallersteiner[7] made a study of the basal and nitrogenous metabolism under carefully controlled conditions, in a series of 19 cases of carcinoma selected because of their freedom from fever, edema and gastro-intestinal disturbances. All were cachectic and anemic. In three of the cases there was a considerable increase in the basal metabolism, the rest showing no appreciable variation. The respiratory quotient was normal in all, indicating the absence of abnormality in the combustion of food. With adequate food intake it was possible to bring all the patients into nitrogenous equilibrium. Rats with transplantable carcinoma were found by Händel and Tadenuma[8] to have a respiratory exchange on the average 10 per cent. lower than the normal control animals; in animals with large tumors the decrease was as much as 20 per cent. They claimed that this lowering of metabolic activity could not be the result of a lower exchange of the tumor tissue, since the respiratory exchange of such tissue had been shown to be higher than that of normal tissues. They interpreted their findings as due to a depressing influence of tumor derivatives on general cellular metabolism. When rats with tumors were subjected to roentgen radiation, the respiratory exchange increased and approached the normal, an effect which the authors explained as due to decrease of the depressing action of tumor products.

Nitrogen Partition of Urine.—Interesting quantitative changes in the nitrogen partition of the urine have been obtained, but always in individuals in whom cachexia was already marked. These differences, as is the case with the total nitrogen excretion, can not be interpreted as characteristic of tumors; they occur in cachexias due to other causes. In carcinoma cachexia, the total urea of the urine may be decreased, forming 80 per cent. of the total nitrogen of the urine, as compared with the normal of 86 to 90 per cent. The other nitrogenous constituents may be increased; uric acid to as high as 5 per cent., as compared with the normal of 0.5 to 1.0 per cent.; and ammonia to as high as 13 per cent., instead of the normal 3 to 5 per cent. Occasionally both uric acid and ammonia form a decreased proportion of the total nitrogen output. The nitrogenous extractives may be markedly increased, figures as high as 13 to 23 per cent., instead of the normal 7.0 to 12.0 per cent., being reported.

While the alterations given above are quite striking, it is to be noted that a comparison with normal figures is difficult, because the latter themselves vary so greatly and are dependent upon the nitrogenous intake. Thus Folin[9] gave the following extremes in normal individuals on a high nitrogenous diet and on a very low intake:

	High N Intake	Low N Intake
Total nitrogen	14.8–18.2 gm.	4.4– 8.0 gm.
Urea nitrogen	86.3–89.4 per cent.	62.0–80.4 per cent.
Ammonia nitrogen	3.3– 5.1 per cent.	4.2–11.7 per cent.
Creatinine nitrogen	3.2– 4.5 per cent.	5.5–11.1 per cent.
Uric acid nitrogen	0.5– 1.0 per cent.	1.2– 2.4 per cent.
Undetermined nitrogen	2.7– 5.3 per cent.	4.8–14.6 per cent.

Of further interest are Hammarsten's[10] comparative figures for normal adults and infants:

	Adults, Per cent.	Infants, Per cent.
Urea nitrogen	84–91	73–76
Ammonia nitrogen	2– 5	7.8– 9.6
Uric acid nitrogen	1– 3	3.0– 8.5
Extractives nitrogen	7–12	7.3–14.7

It is evident that the changes in nitrogenous excretion described in tumor cachexia are of the same nature and of about the same degree as those which occur in normal adults on a low nitrogen intake, which is apt to be the condition that prevails in the cachectic tumor host, and in infants with their relatively lower intake.

Saxl[11] maintained that the metabolism of the precursors of urea is disturbed and incomplete in cancer, the urea formation being consequently decreased. The urea decrease has been ascribed by some investigators to involvement of the liver; others have considered it characteristic of the presence of tumor wherever situated. Increased uric acid excretion, when present, appears to be associated with leukocytic infiltration and destruction of tumor tissue. Ammonia increase in tumors is usually seen only in cases of advanced cachexia, and appears to be the result of the latter. Saxl[11] interpreted the increased ammonia output as an evidence of acidosis, due to incompletely oxidized acid protein derivatives. Robin[12] could find no constant variations in the ammonia or amino-acid excretion in patients with malignant tumors. The increase in extractive nitrogen is believed to be due to destruction of tumor tissue or to be a late manifestation of undernutrition and cachexia.

The observed changes in the nitrogen partition of the urine are open to criticism because of lack of dietary control and because the range of variation in normals under extreme variations in intake may be even greater than that which has been found in tumor bearing individuals. Ordway and Morris,[13] who attempted to overcome the objection of inadequate control by studying the nitrogenous excretion of rats with transplantable sarcoma in comparison with normal animals of the same age, both being maintained on the same controlled diet, found the uric acid "markedly" increased in animals with rapidly growing tumors, and noted a "distinct" increase of creatine and a diminution of creatinine. Their diet of ordinary soda biscuit and water must be considered a poor one in view of our later greatly increased knowledge of what constitutes an adequate diet for the animal used. Even if the alterations noted in the urinary nitrogen partition of tumor individuals were more uniform than they have actually been found to be, it is doubtful whether they would prove what they have been supposed to establish, namely, that the abnormal metabolism of the tumor tissue is the cause of the tumor cachexia. It is much more probable that the alterations are the result of the cachexia, rather than an evidence of a disturbed metabolism which is the cause of the cachexia.

Neutral Sulphur and Colloidal Nitrogen of Urine.—Changes in the quantity and in the composition of the undetermined or rest nitrogen fraction of the urine have been the subject of much study, and have been believed to be more important than changes in nitrogen partition. Töpfer, according to Saxl,[11] in 1892 reported an increase in the residual nitrogen of the urine of cancer patients and believed the increase to be due to some unknown nitrogen-containing fraction. It was shown by Salomon and Saxl[14] that the increase was due largely to oxyproteic acid, the nitrogen of which they claimed constituted a maximum of 2.1 per cent. of the total nitrogen in normal urine and a minimum of 2.5 per cent. in the urine of cancer patients. Somewhat later[15] they also determined a decided increase of the easily oxidized portion of the neutral sulphur of the urine; the increase, which was partly accounted for by the oxyproteic acid, was ascribed to incomplete protein metabolism and was held to be of diagnostic importance. The urinary colloidal nitrogen was found increased by Salkowski[16] from a normal average, as determined by the method finally adopted, of 1.22 per cent. of the total nitrogen to an average of 3.03 per cent. in 10 cases of carcinoma. In the latter group, the minimum of 2.15 per cent. was greater than the maximum of the normal group; the maximum of the tumor group was 4.62 per cent. Salkowski's pupil, Kojo,[17] who perfected the method of precipitating the colloidal nitrogen, claimed that the colloidal nitrogen fraction was not identical with the fraction which contains the oxyproteic acid; in the former he found uric acid.

The increases in residual and colloidal nitrogen and in neutral sulphur were so striking that they at once assumed importance as aids in the diagnosis of malignant tumors. Pasetti[18] determined the neutral sulphur of the urine by the method of

Salomon and Saxl in 200 subjects, of whom 46 were cases of malignant tumor. He found the increase noted by Salomon and Saxl in 68.7 per cent. of cases with carcinoma and in 35.7 per cent. of sarcoma cases. In 84 to 89 per cent. of persons without cancer there was no increase. A number of other observers found the sulphur reaction of Salomon and Saxl positive in cancer, but the accumulation of data gave evidence of a similar increase in cachexias of other origin. Greenwald[19] could detect no difference in the urine of carcinoma patients as compared with that of normals and of patients with diseases other than carcinoma; he concluded that the test has no diagnostic value. Damask[20] used a method which he claimed precipitated only oxyproteic acid. He found that the nitrogen of this substance constituted 1.5 to 2.7 per cent. of the total nitrogen in non-cancer patients. In 35 of 42 certain cases of carcinoma, the figures ranged from 2.8 to 4.7 per cent.; in five cases the percentage was lower than normal. One of three pregnant women and four of 45 cases of tuberculosis gave figures falling within the carcinoma range, the rest of the controls being within normal limits. Semenow[21] found an increase in the colloidal nitrogen of the urine of cancer patients, as described by Salkowski and Kojo. But he also found an equal increase in a variety of other conditions, as acute appendicitis, acute endocarditis, anemia, diabetes, and tuberculosis. deBloeme, Swart and Terwen[22] determined an increase in the amount of the non-dialyzable portion of the colloidal nitrogen precipitate by the Kojo method, as compared with normal urine, but found no increase in the colloidal nitrogen itself. The results of Goodridge and Kahn[23] indicated that neither the Salomon and Saxl sulphur reaction nor the Salkowski colloidal nitrogen test had the diagnostic importance ascribed to them by many previous writers.

F. Mülller[1] claimed that 25 per cent. of carcinomatous individuals excrete albumin in the urine, and v. Noorden[24] placed the figure as high as 72 per cent. The latter also noted the appearance of albumose in the urine when tumors undergo necrosis. Falk, Salomon and Saxl[25] found an increased excretion of polypeptides by means of the formol titration method. Killian and Kast,[26] as a result of study of the chemical changes in the blood, claimed that there is evidence of renal damage in many cases of malignancy. The excretion of albumin and the other abnormalities in urinary composition may be due, in part at least, to this factor. Other urinary abnormalities which have been described, but always at the end stage of cachexia, are an increase in urobilin and in the ketone bodies. The increase in urobilin, according to Braunstein,[27] need not be associated with detectable icterus.

Mineral Excretion.—V. Moraczewski[6] and others studied the mineral excretion in cancer. An increased output of the mineral constituents has been found, although the sodium content of the urine may be decreased in carcinomatous cachexia. Retention of chlorid occurred in the cases studied by Glosser and Frisbie.[2] The decreased sodium chlorid excretion was believed by F. Müller[1] to be due to decreased food intake, and by v. Noorden[24] to the destruction of body tissues poor in this salt. In the terminal cachexia it may be associated with water retention, the faulty chlorid elimination being caused by impaired renal function.

That the metabolism in advanced cancer deviates from normal is evident from the clinical condition of the patient and from the quantitative and qualitative alterations in the excretion of the end products of metabolism described by many. The inconstancy of the chemical findings, however, makes an understanding of the nature of the metabolic disturbance difficult. Saxl[11] interpreted all the urinary chemical changes as evidence of abnormal and incomplete oxidation of protein; whether the protein involved is that of the tumor or of the host tissues is immaterial. The closest analogy to an altered metabolism like that of cancer, associated with decreased oxidation, is that which follows experimental intoxication over a period of time by hydrocyanic acid and its compounds. Edinger and Clemens, and Mayer, according to Saxl, brought about an increase in the total protein metabolism, associated with augmented excretion of ammonia and of neutral sulphur, by administration to human beings over a period of two or more days of small doses (0.25 to 1.0 gm.) of potassium sulphocyanide. The resulting metabolic disturbance they believed to be due to the formation of minute amounts of hydrocyanic acid in the intermediary metabolism of the proteins. Saxl,[11] after the administration of 1.5 to 2.0 gm. of sulphocyanide in two or three doses to three subjects without tumor, observed an increased urinary excretion of the substance over many days, an increase in the oxyproteic acid nitrogen portion of the total nitrogen of 206 to 270 per cent., and the development of a positive neutral sulphur reaction, the latter not to be explained by the sulphur ingested with the sulphocyanide. Such findings, similar to those which he considered characteristic of cancer, led him to make quantitative determinations of the potassium sulphocyanide excretion in the urine of 23 patients with malignant tumors and of 20 normals and patients free of tumor. In the latter group the total 24-hour excretion varied from a minimum of 33.5 mg. to a maximum of 202.4 mg., with an average of 90.3 mg. In the tumor group, the minimum excretion was 72.5 mg., the maximum 232.8 mg., with an average of 202.8 mg.; a case of questionable carcinoma of the stomach, with an excretion of 28 mg., is excluded. Alternate overfeeding and starvation of a dog led to no appreciable change in excretion, and in the control series of human beings with fever, cachexia or anemia, the excretion was below the average for the group, warranting the conclusion that inanition, fever, cachexia, and anemia can not be the cause of the increased sulphocyanide excretion observed in cancer patients. Both Lang and Hejmann, according to Saxl, had found an increased excretion of sulphocyanide in hydrocyanic acid intoxication, and interpreted the increase as the result of a detoxication process. Saxl could not detect a higher sulphocyanide content of the tumor tissues, as compared with normal tissues. The experimental work of Saxl and his finding of a decidedly increased excretion of sulphocyanide in cancer are suggestive of abnormal metabolic processes in this disease, which are associated with the formation of toxic substances, possibly cyanogen compounds.

Attempts to reproduce cachexia experimentally and to prove a specific toxic action of tumor tissue by the injection of material derived from tumors are open to the objection that the protein split products of normal tissues may be highly toxic. Boyksen[28] produced a progressive loss of weight in rabbits by the intravenous injection of extracts of macerated tumor tissue. A nucleoprotein prepared by Burnett[29] from the Flexner-Jobling rat carcinoma was highly toxic for rabbits on intravenous injection. Such results do not prove the existence of a specific tumor toxin; they merely indicate that the degradation products of tumor tissue may have a toxic action.

The study of the metabolism in cancer has yielded no facts which permit definite deductions as to the rôle of neoplasia in the general economy of the body, or as to the chemical processes going on in the tumor itself. Such changes as have been noted have usually been associated with advanced cachexia, but that they are indicative of the processes which cause the cachexia still remains to be established. Diminished oxidation and increased destruction of body protein, due to a variety of causes, may result in metabolic alterations identical with those found in tumors. Such alterations as have been detected may be the result of cachexia, rather than its cause, and may be no more characteristic of the metabolism of an individual with a tumor than that of one with an equal degree of cachexia due to any cause. We must conclude, with Lewin,[30] that chemical study of the metabolism in malignancy has not established that a specific cachexia occurs in malignant disease, and that it has carried us no nearer a solution of the cancer problem than have other lines of research.

Changes in the Blood.—Anemia.—Secondary anemia is the rule in the terminal stage of many tumors. While the anemia has been ascribed by many to a specific cancer toxin the proof of the existence or action of such a toxin is upon the same indefinite footing as the causation of cachexia by tumor. Although a hemolytic action of extracts of tumor tissue has been described by a number of investigators, anemia, like the chemical changes noted, appears to be a result of cachexia. Kabierske[31] studied the progress of the anemia in mice with transplantable carcinoma. He considered it a secondary anemia identical with that in human beings with tumor and probably due to toxins absorbed from the tumor tissue. He found the resistance of the erythrocytes somewhat decreased. Cohnreich[32] criticized the usual method for determining the resistance of the red blood cells; by means of a modified method he found the resistance somewhat increased in carcinoma. Jaffé[33] found the coagulation time of the blood increased in five cases of sarcoma, but within normal limits in six cases of carcinoma. He explained this difference upon the basis of the vascular relations in sarcoma, which permit the more ready entry of sarcoma juices into the blood stream.

Blood Chemistry.—Chemical changes in the blood have been studied by many observers, but the results are quite contradictory.

Sugar.—Benedict and Lewis[34] found the blood sugar increased in 36 per cent. of 53 cancer patients studied. Rhodenburg, Bernhard and Krehbiel[35] obtained normal blood-sugar values, but found the hyperglycemia following glucose ingestion to be greater and more prolonged in cancer patients than in normal individuals. The decreased sugar tolerance was characterized by a blood-sugar curve which ran a course intermediate between the curves of normals and diabetics. The hyperglycemic reaction following the injection of homologous proteins they[36] found to be less marked in cancer cases than in persons free of tumor. Friedenwald and Grove,[37] from a study of 32 cases of gastro-intestinal carcinoma, claimed that the fasting blood sugar level was higher in this form of cancer than in other forms or in normals, and that the decreased sugar tolerance curve after glucose ingestion was distinctive enough to give it differential value in diagnosis. de Niord and Schreiner[38] could find "nothing especially characteristic of either the blood sugar or diastase of the cancer patient at any stage of his disease." Theis and Stone[39] found an increase in blood sugar in 26 per cent. of 189 cases of malignancy studied by them, and a decrease below normal in 13 per cent. In a series of 119 tumor cases, Killian and Kast[26] could determine no increase in blood sugar or decrease in tolerance, unless there was evidence of renal impairment. By the picric acid method for estimating reducing substance of the blood Leyton and Leyton[40] found a definite increase, which they held to be of value in differentiating malignant disease from other conditions. They believed that the method as used by them detected other reducing substances in addition to glucose.

Urea and Non-protein Nitrogen.—Theis and Stone[39] found the blood urea and non-protein nitrogen low in their series of cases. They believed that the renal element was not a factor in this decrease, and by analogy with the reported low non-protein nitrogenous content of the blood in pregnancy, intimated that the decrease is due to the growth demands of the tumor tissue.

Protein.—Theis,[41] in a later study of 27 tumor cases, could observe no consistent changes in the total blood proteins. The wide variations observed in the protein content of whole blood are explained by the differences in hemoglobin content. The protein content of the serum in 13 cases varied from 6.0 to 8.2 per cent., and in the plasma of 14 cases from 5.1 to 8.1 per cent., variations no greater than those found in 16 non-tumor cases. Loebner,[42] in 44 cases, found serum protein figures of 4.2 to 9.0 per cent., with an average of 7.3 per cent. Robin[43] found an increase in the albuminoid nitrogen of the serum in cancer. Loeper[44] and his co-workers claimed that the increase in total protein of the blood serum which they observed in cases of malignancy is due to an increase of the globulin fraction, the serum albumin being proportionately decreased. They found normal figures of 7.8 to 8.0 gm. of protein per 100 c.c. of blood, globulin constituting 35 per cent. and albumin 65 per cent. Of 18 carcinoma cases, nine showed an increase in serum proteins, the values ranging from 8.05 to 9.2 per cent. In three carcinoma cases, in which globulin and serum albumin were determined separately, the former constituted from 51 to 75 per cent. of the total protein, the serum albumin from 25 to 49 per cent. The relative and absolute increase of globulin they ascribed to the absorption of tumor protein by the blood, and attempted to prove their assertion by the use of the anaphylactic reaction[45] and by a study of the changes which followed radiation[46] of tumors. The results of their anaphylactic experiments can not be said to establish their point. The figures obtained in six cases of carcinoma before radiation vitiate their earlier findings of an increase in total serum protein, since they showed only 5.5 to 7.3 per cent. of protein. In five of the cases examined two days after radiation the total protein had increased 3.5 to 12.5 gm. per 100 c.c. In the sixth case, examined six days after radiation, there was a decrease from the original 6.6 per cent. to 5.8 per cent. In the cases showing an increase after radiation, the serum albumin remained fairly constant, whereas the globulin increased, which the authors interpret as proof of absorption of tumor protein, the increase in these cases being due to the destruction of tumor tissue by radiation.

Kennaway[47] has recently published his findings, based upon 122 serum protein estimations in 104 cases of all kinds. While he found that some advanced cases of carcinoma showed an increase in globulin greater than occurred in other conditions, other cases equally advanced failed to show this change. The globulin fraction constituted from 30 to over 55 per cent. of the serum protein; he believed that the increase, when present, was the result of a breaking down of tumor tissue. The decrease in serum albumin, which was proportional to the increase in globulin, he interpreted as probably a compensatory effect, the purpose of which was the maintenance of the viscosity of the blood within normal limits. Kennaway did not believe that the changes which occur could have the diagnostic importance ascribed to them, since they occur only late in the disease.

Uric Acid.—Killian and Kast,[26] in their 119 cases, found a definite increase in the uric acid concentration of the blood in 80 per cent., and of the urea nitrogen and creatinine in 60 per cent. They explained the increase by damage to the kidneys, brought about by the tumor, an explanation which they believed holds also for the increase in blood sugar which has been reported.

Cholesterol.—Robertson and Burnett,[48] by injecting lecithin or cholesterol directly into the transplanted, growing carcinomas of rats, found that cholesterol stimulated tumor growth and hastened metastasis, whereas lecithin retarded growth and diminished the tendency to metastasis. In nine cases of cancer, Luden[49] found a blood cholesterol variation of from 0.26 to 0.71 per cent., 0.27 per cent. being accepted by her as the average in normals; the lower values in the tumor series occurred in cases which had been treated by radiation. In Denis'[50] series of fourteen cases, the cholesterol figures were within the range of normal variation except in one case, in which the content was low and was associated with anemia.

The discordant blood cholesterol figures may find their explanation in recent work reported by Currie,[51] who observed a distinct seasonal variation in the average blood cholesterol content of normal individuals, as follows: November to January 0.11 per cent.; February to April, 0.18 per cent.; May to July, 0.28 per cent.; August to October, 0.18 per cent. In tumor cases, in which the seasonal variation was kept in mind, he found the following: November to January, 16 determinations in 16 cases, an average of 0.077 per cent., with a maximum of 0.10 per cent. and a minimum of 0.07 per cent.; February to April, 23 determinations in 21 cases, an average of 0.14 per cent., with a maximum of 0.28 per cent. and a minimum of 0.076 per cent.; May to July, 22 determinations in 21 cases, an average of 0.22 per cent., with a maximum of 0.30 and a minimum of 0.12 per cent.; August to October, 17 determinations in 17 cases, an average of 0.15 per cent., with a maximum of 0.23 and a minimum of 0.11 per cent. His averages indicate a slight degree of hypocholesterolemia. Most of the tumors examined by him were epithelial. His tables exhibit no regular differences as between sarcoma and carcinoma, or as between tumors of rapid and of slower growth.

Reaction.—Peiper[52] observed a decrease in the alkalinity of the blood in carcinoma, but this finding is at variance with later results obtained by more accurate methods. Moore and Wilson,[53] by titration methods, found that both the serum and the serum ash of cancer patients required a slightly greater amount of standard acid for neutralization. Watson[54] obtained confirmatory results, except in advanced tumor cachexia. Sturrock,[55] who used the same titration method employed by Moore and Wilson and by Watson, found that normal serums required on an average of 0.173 c.c. of normal acid for neutralization, and cancer serums an average of 0.190 c.c.; he considered anything over 0.200 c.c. prresumptive evidence of carcinoma. In all the above work the blood was allowed to clot and stand for 24 hours, and no provision was made to prevent a loss of carbon dioxid.

Menten[56] determined the hydrogen-ion concentration of the blood serum of 72 cases of malignancy by the gas-chain method. For 12 normal individuals an average pH value of 7.93 was found, the extremes being 7.91 and 8.02. In the 72 tumor cases the average pH was 8.08, the extremes being 7.94 and 8.44. Of the entire group, only 11 had a pH reading of less than 8.00, and only one, a superficial epithelioma of the lip with a reading of 7.89, had a lower hydrogen-ion concentration than the average for the normals. Eight of the readings below pH 8.00 occurred in a group of 36 epitheliomas of the skin and buccal mucosa, for which the average figure was pH 8.013. The increased alkalinity could not be correlated by Menten with anemia. It is to be noted that Menten's normal figures are considerably higher than those generally accepted. This discrepancy may be accounted for by the fact that she made no provision to prevent the escape of carbon dioxid from the serum. Although this error in technique vitiates all her results, the uniform increase found in tumor cases is significant, if we may believe that the increase due to the escape of carbon dioxid was proportional in both normal and tumor serums. Killian and Kast,[26] who determined the carbon dioxid combining capacity in their series, could find no evidence of increased alkalinity. When there was nitrogen retention, which, as noted above, they believed to be due to renal damage through the tumor, then the alkalinity was decreased.

Chambers,[57] by colorimetric methods, determined the hydrogen-ion concentration of the dialysate of whole blood, using precautions to prevent the loss of carbon dioxid. In 45 cases of carcinoma he found the dialysate to be "distinctly more alkaline," the average being pH 7.45, as compared with an average of pH 7.31 for normal controls. No relationship to anemia could be established. Chambers and Kleinschmidt[58] determined the hydrogen-ion concentration from the carbon dioxid-bicarbonate ratio of the blood. The average for 12 normals was pH 7.29; of eight determinations in diseases other than carcinoma, pH 7.33; and of 23 determinations in carcinoma, pH 7.34. The alkalosis of the dialysate of cancer plasma, as compared with the practically normal reaction of the blood by the second method, they ascribed to an increase in non-diffusible anions in the plasma.

Mineral Constituents of the Blood.—V. Moraczewski[59] found an increase in the total chlorine content of the blood, associated with a decrease in phosphorus. Similar changes were detected in chlorosis and were not, therefore, considered characteristic of carcinoma, although retention of sodium chlorid occurred with a higher hemoglobin content in cancer than in chlorosis. Rhodenburg and Krehbiel[60] have recently attempted to correlate the changes in the mineral constituents of the blood with those in tumor tissue, using rats with transplantable tumors. They found that the developmental period of such tumors is associated with a decrease in the salt content of the blood and of the normal tissues. This "demineralization" is apparently due to the greater demands of the tumor cells for inorganic salts. When the tumor cells die, their salts are liberated and are rapidly taken up by the blood and tissues. These investigators did not believe that changes in salt metabolism influence the origin of tumors, and concluded "that the changes observed are secondary to cell growth and death, and bear no relationship to the biologic character of the cells which grow or die." In still later work they[61] concluded that the changes found are not the result of an increased affinity of growing transplanted cells for mineral salts, since the changes are relative. Potassium is increased more than sodium in the growing tumor tissue during the stage of demineralization of the blood, whereas the sodium of the blood is increased more than the potassium during the stage of hypermineralization of the blood.

Phosphorus.—V. Moraczewski[59] had described variations in the phosphorus content of the blood, but he had correlated these with the anemia of tumor cachexia. When the erythrocyte count was low, the phosphorus content was low, but it was equally low in non-malignant anemias of equal grade. Gröbly[62] believed that the phosphorus syntheses in the tissues are dependent upon nucleoproteid synthesis, and that variations in the tissue phosphorus content give a measure of disturbance of this synthesis. With this idea in view he determined the phosphorus content of the red blood corpuscles, looking upon these as the tissue elements of the blood. The phosphorus content of the corpuscles he correlated with the number of erythrocytes in a phosphorus quotient, which he expressed as $\frac{\text{Mg. } P_2O_5 \text{ per } 100 \text{ c.c. blood}}{\text{Millions of R.B.C. per cm.}}$. He claimed that a phosphorus quotient greater than 3.17 was always associated with malignancy, and that in malignancy the phosphorus content of the corpuscles is increased.

Vorschütz and Vorschütz[63] agreed that the phosphorus quotient is uniformly high in cancer and is of diagnostic value, although the absolute phosphorus content of the blood might be normal. Zerner[64] recognized the parallelism between phosphorus content and erythrocyte count, but maintained that the phosphorus quotient is specifically elevated in malignant disease. Buckman, Minot, Daland and Weld[65] repeated the work of the above investigators and found the total phosphorus content of the blood roughly parallel to the hemoglobin; they concluded that the phosphorus quotient has no diagnostic value.

Calcium.—Krehbiel[66] determined the calcium content of the blood plasma in 34 cases of malignant disease. The values found by him were within the range accepted as normal. No characteristic concentration accompanied any type or localization of tumor. Theis and Benedict,[67] in 13 cases of early and 14 of late malignancy, found the calcium, magnesium and phosphorus to be slightly below the lower limit for normal. Sodium was normal, but potassium was slightly decreased in a large proportion of the cases.

De Niord, Schreiner and de Niord[68] studied the urea, creatine, creatinine, uric acid, chlorids, cholesterol, fatty acids, total fat, sugar, diastatic function, and the corpuscle and plasma percentage of the blood in 41 cases of carcinoma before and after roentgen radiation. Urea, creatine and creatinine showed nothing characteristic of cancer, either before or after radiation. Uric acid was moderately increased after exposure; the increase was believed to be due to nuclear degeneration, and was not considered characteristic of malignancy. Sodium chlorid was not altered from normal by the presence of tumor or by the rays. Cholesterol, fatty acids and total fats were generally increased before radiation. The cholesterol content was increased still further by the exposure, presumably as the result of cell autolysis. The increased content of fatty acids and total fats was reduced by the rays. The blood sugar and diastatic activity showed nothing characteristic of carcinoma; in some of the cases, the diastase was activated above the normal by the exposure. Plasma and corpuscle percentages were not altered by radiation.

From the above survey of the chemical changes in the blood in malignancy, it is evident that no consistent results have been obtained. The most striking finding is the increased alkalinity observed by Menten[56] and by Chambers;[57] but here also the discordant results of Killian and Kast[26] make interpretation difficult. It is to be hoped that further refinement of chemical methods will ultimately yield results of value in the study of tumors before the stage of cachexia has been reached. Chemical changes associated with massive necrosis of tumor tissue, either spontaneous or as the result of radiation, if such chemical alterations should be found to occur, will still leave unanswered the old question of the relation of tumor metabolism to cachexia.

Chemistry of Tumor Tissues.—*A priori* reasoning would lead us to suspect that the well-differentiated tissues of slowly growing benign tumors might show little variation in their chemical make-up from the corresponding normal tissues, since the histologic structure is so similar in benign tumors and in normal tissues, and since cellular structure and differentiation are, after all, merely the morphologic expression of chemical composition. The same kind of reasoning would lead us to suppose quite marked differences in the chemical constituents of undifferentiated malignant tumors, since the latter differ so markedly in morphology from any normal tissue. The expected chemical similarity between benign tumors and their corresponding normal tissues is a fact, but no great chemical dissimilarity as between malignant tumor and normal tissues has been found.

Of the benign tumors, it may be said in general that chemically they are quite like their homologous normal tissues. Thus, lipomas are identical in composition with the subcutaneous adipose tissue in which they may arise. Nucleoproteins and purines were found by Wells and Long[69] to be low in benign tumor tissues, as they are in adult tissues. In the malignant tumors, the proportion of nucleoproteins is higher than in benign tumors or in normal tissues, but the content is not so high as one would expect from the greater richness of malignant tissues in nuclei. This difference probably depends upon the greater fluid content of the younger tumor nuclei. An increased water content was determined by Hirsch and Wells[70] in a retroperitoneal liposarcoma with myxosarcomatous areas. Very little mucin was present, indicating that the myxomatous condition was due to edema. Wolter[71] and Robin[72] found the water content of carcinoma of the liver increased as compared with the surrounding tissue.

Nitrogen.—The total nitrogen of fresh tumor was found by Chisolm[73] to be lower than that of normal tissues. In the dried material there was little difference, indicating that the lower nitrogen of fresh tumor is due to a higher water content. In five carcinomas of the liver analyzed by Robin[72] the water content of the neoplastic tissue was greater than that of the surrounding liver and the total nitrogen was lower. In carcinoma a larger bulk of histologic substance is constructed out of a smaller amount of material than is the case in the normally differentiated tissues. The lower nitrogen quantity related to the soluble nitrogen; the insoluble nitrogen was increased in the tumor tissue. The proteolytic activity of the immediately surrounding liver tissue was two or three times as great as in the tumor, which led Robin to believe that a neoplasm derives its materials for growth from the normal tissue by autolysis of the latter. Growth of a tumor becomes possible through preparation of the soil by the action of proteolytic enzymes on the tissue in which the tumor grows. Those chemical compounds which represent the intercellular and other tissue derivatives are lower or absent in malignant tumors, as compared with normal tissues or benign tumors.

Proteins.—The proteins and the distribution of their amino compounds appear to be identical in neoplastic and in normal tissues, as determined by the studies of Bergell and Dörpinhgaus,[74] Bergell,[75] Neuberg,[76] Drummond[77] and others. Such percentage differences as occur among the amino compounds of tumors are to be correlated with the nature of the tissue from which the tumors are derived, or with the younger, more cellular character of the tumor. According to Drummond,[78] tumor protein contains a higher proportion of diamino-acids than that of normal tissues, the percentage being greater in more rapidly growing, cellular neoplasms than in slowly growing ones. He did not believe that the increased content of hexone bases was responsible for the greater rate of cell division. The presence of amino-acids in the non-hydrolyzed tissue Drummond ascribed to autolysis. Fasal[79] determined a considerable increase in the tryptophane of an epithelioma of the skin, secondary carcinoma of the liver, mouse and rat carcinoma, but no increase in scirrhous carcinoma of the breast. He concluded that certain tumors are able to enrich themselves at the expense of the rest of the body, and that other tumors do not use tryptophane and appear to be composed of proteins of lower value. Kocher[80] found the hexone bases increased 100 per cent. and more in five tumors analyzed; the increase was chiefly in arginine, lysine and histidine. Since the tissues can not synthesize these necessary growth substances, the increase was taken to indicate that normal tissues are broken down to form the required diamino-acids for the growing tumor tissue. Long[81] found the purines of tumors to be the same as those of normal tissue. Guanine and adenine were present in largest amounts, and xanthine and hypoxanthine in only small quantities; uric acid was absent.

Glycogen.—An unusually high glycogen content has been considered characteristic of tumors, and by some the malignancy of tumors has been held to be directly proportional to the richness in this carbohydrate. Glycogen is not, however, a specific tumor component, but occurs in normal embryonic and proliferating tissues; in the latter, as in tumors, it is an evidence of high metabolic activity. Glycogen tends also to accumulate in tissues which are undergoing degeneration through impaired nutrition; it may, therefore, be present in tumors whose cells are degenerating or dying. Lubarsch,[82] who studied the presence of glycogen in tumors by microscopic rather than by quantitative chemical methods, found this material to be present in 29 per cent. of the 1544 tumors examined. It occurred in only 1.1 per cent. of the 444 benign tumors, in 43.6 per cent. of carcinomas, in 70 per cent. of sarcomas, and in all the teratomas, rhabdomyomas, hypernephromas, and syncytiomas.

Cholesterol.—Bennett[83] found that the cholesterol of the Flexner-Jobling rat carcinoma increased with the age of the tumor, and that the actively growing, peripheral portions contained less than the central portion. Subcutaneous injection of cholesterol did not increase "very markedly" the amount of this substance present in the tumor.

Inorganic Constituents.—Of inorganic constituents, potassium is high in rapidly growing tumors, as it is in young normal tissues. Calcium is low in young tumors, but increases in amount in older ones, and may become so great as to be deposited in insoluble form when necrobiosis occurs (Wells).[84] Waterman[85] found the calcium content to be proportional to the degenerative changes present. In growing tumors the quantitative relationships of calcium to potassium and sodium, as determined by Clowes and Frisbie[86] and by Beebe,[87] suggest an antagonistic action between the last two ions and calcium in relation to growth. In experiments upon transplantable mouse carcinoma, Cramer[88] found that exposure of the tumor to calcium chlorid *in vitro* caused a distinct retardation of growth; this inhibitory action could be set aside by sodium ions. Sugiura, Noyes and Falk[89] also obtained marked inhibition of growth when rat carcinoma transplants were subjected to the action of calcium chlorid. Rhodenburg and Krehbiel[60,61] found the potassium and sodium content of actively growing transplantable rat tumors high, the potassium being increased relatively more than the sodium.

The content of phosphorus and iron is proportional to the nuclear content of the tumor tissue. Robin and Bournigault's[90] analyses of carcinoma of the liver showed a considerably lower content of total sulphur in the tumor than in the surrounding normal liver tissue.

Specific Constituents.—Tumors derived from normal tissues, which contain peculiar constituents or unusually high amounts of certain compounds, are also apt to have a similar composition. Wells[91] found a high fat and lipoid content in hypernephromas, corresponding to that of the normal adrenal. Liver carcinoma metastases may contain bile (Wells).[92] Iodin was found to be present in the metastases of thyroid carcinomas by Carlson;[93] Marine and Johnson,[94] however, found that thyroid carcinoma and its metastases had lost the power of storing administered iodin, a property which is characteristic of normal thyroid tissue.

Oxygen Consumption.—If the metabolism of growing tumor tissue is higher than that of normal tissue, as is suggested by the rate of growth and the younger character of the former, the oxygen consumption should be increased. Russell and Gye[95] compared the oxygen consumption of normal and cancerous mouse tissues *in vitro*, and found it higher in the latter than in the former; the consumption increased with rapidity of growth of the tumor. Russell and Woglom[96] studied the respiratory exchange of mouse carcinoma. The results indicated that the more rapidly growing tumors derive their energy largely from carbohydrates, more slowly growing ones from fats. The greater utilization of carbohydrate by the younger tissue is in accord with the greater richness of such tissue in glycogen. Fleisch,[97] who compared the oxygen consumption of Jensen's rat sarcoma with that of muscle of the same animal, found a lower initial velocity of oxygen uptake in the case of the tumor, but the total amount of oxygen taken up was greater, weight for weight, by the sarcoma than the muscle.

Nutrition and Tumor Growth.—The chemical composition of tumor tissue is probably directly dependent upon its metabolic activities, and the relation of the latter to those of the body as a whole is a matter of interest. The persistence of lipomas in spite of the disappearance of the body fat in starvation, and the progressive growth of malignant tumors in spite of extreme inanition, point to a great degree of metabolic independence upon the part of tumors. The work of Robin,[72] Drummond,[78] Fasal,[79] and Kocher,[80] noted above, also leads to the conclusion that neoplasms are not dependent upon the food intake of the body for their growth materials, but are able to derive them from the host tissues themselves by proteolytic destruction of the latter.

Attempts to study experimentally the effect of body nutrition upon tumor growth have led to conflicting results. Moreschi[98] subjected mice, into which a rapidly growing mouse sarcoma had been transplanted, to overfeeding and to varying degrees of underfeeding. He claimed that the growth of the tumors was proportional to the nourishment of the ainmals. The net weight of the latter decreased progressively, in both overfed and underfed mice, indicating that the weight of the host is influenced adversely not only by inadequate intake, but also by withdrawal from the host tissues of substances necessary for tumor growth. Dietary restriction, if not too extreme, slowed the growth of the tumors and prolonged the life of the animals. Marked restriction before inoculation prevented or retarded the development of the implanted tumors. Sweet, Corson-White and Saxon[99] worked with rats and mice with transplanted tumors, comparing the results of transplantation into animals on a restricted, growth limiting diet and on a full diet. They found that the restricted diet "markedly reduced" the number of successful transplantations, rendered the rate of growth of the tumors "much slower," and increased the number of retrogressive tumors. Rous,[100] who tried to attack the problem of the effect of diet in the same way, concluded that the transplantation method is unsatisfactory. He therefore tried the effect of restriction of diet on the spontaneous mammary carcinoma of mice. Of 130 female animals with such tumors, half were kept on a full diet and half on a restricted diet like that used by Sweet, Corson-White and Saxon. The greater portion of the tumor of each animal of the two series was then surgically removed, with the exception of a small bit, whose blood supply was disturbed as little as possible; at the same time two subcutaneous transplantations from its own tumor were made into each animal. The animals were then observed for a period of five weeks, during which time they were kept upon the original diets. The object of the procedure was to determine the effect of the restriction of diet upon recurrence and metastasis of the original tumors and upon growth of the implants. Recurrence occurred in 83 per cent. of the full-fed animals and in only 41 per cent. of the under-fed ones. The grafts grew in 61 per cent. of the full-fed mice and in 41 per cent. of the under-fed. Rous concluded that the restricted diet had "a very marked influence to delay the reappearance of spontaneous mouse tumors." Drummond[101] claimed that factors which retard the growth of normal animals, such as low protein intake and vitamin deficiency, do not retard the growth of the tumors of the animals. Sugiura and Benedict[102] studied the effect upon transplanted carcinoma of 32 different inorganic salts added in varying proportions to the basal diet. Copper sulphate, arsenic trioxid, potassium carbonate, and calcium chlorid had a retarding influence, but their action in this respect was not marked, copper sulphate being most effective and appearing to have some slight immunizing effect. Certain salts which had a highly toxic action on the rat (tellurium nitrate and selenic acid) had no retarding influence on the tumors. Magnesium carbonate and magnesium chlorid had a "slight but distinct accelerating influence upon the tumor growth." Händel[103] found that a diet poor in salts had no effect on transplanted mouse carcinoma. High potassium feeding increased the percentage of "takes" and accelerated the growth of the tumors. Increased calcium feeding decreased slightly the percentage of "takes" and the growth of the tumors. High phosphate feeding had no effect. Händel and Tadenuma[104] claimed that feeding with an enriched carbohydrate diet caused more rapid growth of transplanted rat carcinomas than high protein feeding.

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DIAGNOSTIC REACTIONS AND ENZYMES OF TUMORS

Diagnostic Reactions.—Physical-chemical and immunologic changes, and alterations of the ferment activity of the blood have been described, and have raised hopes in regard to specific diagnostic reactions. Such reactions have not, however, lived up to the claims made for them by their discoverers, and a specific diagnostic tumor reaction still remains to be found. What we know of the chemistry of tumors and of the reactions of the body as a whole to the presence of tumor leads to the belief that the diagnostic tumor reaction is an *ignis fatuus.*

Meiostagmin Reaction.—Interaction of antigen and specific antibody leads to a decrease of surface tension of the serum in which the interaction occurs. This meiostagmin reaction, first described by Ascoli[1] in 1910, as an aid in the study of immunologic reactions, was believed to be highly specific and to detect the presence of antigen in very high dilution. A similar degree of specificity was claimed by Ascoli and Izar[2] for the meiostagmin reaction when applied to the blood serum of cancer patients. Izar[3] and his colleagues, in further work, showed that the tumor extract could be replaced as antigen by a number of organic chemical solutions, a fact which began to cast doubt upon the specificity of the reaction. Blumenthal,[4] in a critical review, concluded that the phenomenon is not the result of antibody-antigen reaction, but is dependent upon physical-chemical changes which may occur in a variety of pathologic conditions. Differences in surface tension, which the meiostagmin reaction measures, are probably the result of variations in the dispersion of the serum colloids, brought about by lipoids. In a recent (1924) review of the meiostagmin reaction in tumors, Ascoli[5] himself admits that the reaction is not biologically specific, but that it may be useful in gaining further knowledge of disturbances of lipoid metabolism in neoplastic and other diseases. The reaction would appear to depend upon factors other than those due to union of antigen and antibody. As an antigen-antibody phenomenon it can have little value as a specific tumor test, in spite of the fact that it has been found empirically to give a fairly high proportion of positive results in tumors.

Epiphanin Reaction.—Other physical-chemical changes which occur when antigen and antibody unite with each other are believed to form the basis of the epiphanin reaction of Weichardt,[6] namely, a shifting, toward the acid side, of the neutral point of a mixture of barium hydroxide and sulphuric acid when antibody and antigen union occurs in such a mixture. Rosenthal[7] applied this reaction to cancer, and claimed for it a degree of specificity which made it of diagnostic value. Józsa and Tokeoka[8] obtained 81.5 per cent. of positive reactions in 54 cases of clinically certain carcinoma. The majority of 18 cases without tumor gave a negative reaction. Burmeister[9] found the epiphanin reaction to be valueless because of the large number of identical results in the controls.

Complement Fixation.—Following the demonstration of the specific nature of the complement fixation reaction, it was natural to suppose that a similar technical procedure might be of value in the diagnosis of malignant tumor, particularly in view of the value of the reaction in syphilis when a non-specific antigen is used. V. Dungern[10] devised such a reaction, for which he and his pupils claimed positive results in 80 to 91 per cent. of cases. Simon and Thomas,[11] who used an emulsion of medullary carcinoma as antigen in the test, obtained 65 per cent. of positive reactions in 37 cases of malignant disease, and 98 per cent. of negative results in 50 normals and patients free of tumor. The positive reactions continued after surgical removal of the tumor. No logical reason for the reaction as finally modified by v. Dungern[12] can be seen, the antigen being an acetone extract of normal human red blood corpuscles and the serum to be tested being treated with alkali. Coca[13] concluded that the results which have been obtained with this reaction are due in part to accident, in part to summation effects, and in part to uncontrollable factors. Yamanouchi and Lytchkowsky[14] carried out the complement fixation reaction by using as antigen a suspension of a micrococcus which they cultivated from tumor tissue and which they believed to be identical with Doyen's *M. neoformans*. They claimed to obtain positive results in 30 of 37 carcinomas of the breast; syphilis, however, also gave a high percentage of positive reactions.

Anaphylaxis.—Pfeiffer[15] applied the anaphylactic phenomenon to cancer, claiming that the guinea pig can be passively sensitized by injection of blood from cancer patients, so that a reaction occurs when the prepared animal receives an injection of carcinoma extract 24 hours later. Pfeiffer's criterion of an anaphylactic response was a drop in temperature, a reaction which is quite unsatisfactory as an indication of sensitization. Ranzi[16] was unable to obtain true anaphylactic reactions with cancer serums. In a series of 79 cancer patients who received injections of carcinoma material for therapeutic purposes, Coca, Dorrance and Lebredo[17] made no mention of the occurrence of anaphylactic reactions, although they looked upon cancer cachexia as a chronic anaphylactic intoxication due to the continuous absorption of tumor materials and upon pain in tumors as a local allergic phenomenon. V. Dungern[18] described a local cutaneous allergic response following the injection of carcinoma extract into patients with cancer.

Ransohoff[19] described as an anaphylactic response a reaction which was probably anaphylactic when it occurred but which probably had nothing to do with cancer. Guinea pigs were sensitized in pairs, one with normal human serum and the other with the serum of a known carcinoma patient. Two weeks later each received the serum of the suspected carcinoma case. If carcinoma was present the animal sensitized with normal serum developed anaphylaxis, but that which had been sensitized with known carcinoma serum did not. Ransohoff explained this rather paradoxical result by supposing that the blood of cancer patients contains specific substances which immunize the sensitized animal against a later injection of carcinoma serum. The serum of 20 non-malignant cases gave 100 per cent. of anaphylactic responses by this method; 86.7 per cent. of 30 cases of carcinoma failed to react. Green,[20] who repeated this method, could not confirm Ransohoff's findings. With *M. neoformans* antigen he obtained complement fixation, but five of nine non-cancerous cases also gave fixation; as large a percentage of positive results was obtained in both groups of cases if staphylococcus or streptococcus was used as antigen.

Precipitins.—One of the most delicate and specific of all immunologic reactions is the precipitin reaction, which makes possible a differentiation of closely related pure proteins with a greater degree of certainty than is attainable even by chemical methods. The various immunologic reactions discussed above are all based upon the belief that tumor tissues vary sufficiently in composition from the normal tissues of the body to act as antigens and to lead to the formation of antibodies. If this were true, the precipitin reaction might be expected to yield results not attainable by any other method. Engel[21] was one of the first to attempt to apply this reaction to the study of tumors. He immunized rabbits with the blood from carcinoma patients, and then determined the precipitin reaction of the immune serums when united with the serum from the original patients, from others with tumors, and from normal individuals. Although he claimed to obtain more marked precipitation with the serum of the original patients, his results must be considered inconclusive. Mertens[22] next attempted to prepare specific precipitin serums by using tumor extracts for the immunization of animals. His results were negative. An evident criticism of this earlier work is the precipitation which must result from normal serum and tissue proteins, and which might mask any specific tumor reaction. By preliminary absorption of the normal precipitins, Maragliano[23] claimed to obtain specific results in a case of carcinoma of the stomach. Salomon's[24] results with the absorption method were negative. Both of these observers united immune serum and patient's serum. Romkes and Wenckebach[25] obtained precipitation when the serum of a rabbit immunized against carcinoma was permitted to interact with an extract of the tumor, the immune serum being first absorbed with normal human serum. Such a serum also had carcinolytic properties. Coca, Dorrance and Lebredo[17] obtained neither precipitin nor complement fixation reactions in the human cancer cases injected by them with carcinomatous material.

The positive results claimed for the precipitin reaction by a few workers have not been confirmed by a larger number of others who have investigated the matter. One must conclude, either that tumor tissues are so closely related chemically to normal tissues that even the delicate precipitin reaction is unable to differentiate the two, or that the technical procedures thus far tried have not been able to overcome the disturbing effect of the normal proteins which must be present and which may mask any specific effect due to tumor proteins of slightly different composition.

Cytolysis.—Freund and Kaminer[26] found that normal human serum has the property of dissolving suspended cancer cells, that the serum of cancer patients does not have this property, and that cancer serum inhibits the carcinolytic action of normal serum. In later work they[27] attempted an exact chemical explanation of this phenomenon. The lytic action of normal serum they believed to be due to the presence of an ether soluble, nitrogen-, sulphur-, and phosphorus-free fatty acid of high molecular concentration, belonging to the group of saturated dicarboxylic acids, absorbed from the duodenum during the process of digestion. Carcinoma serum did not contain this acid, but contained a substance, at first believed to be a nucleoglobulin but later an unsaturated fatty acid, which counteracts the lytic acid of normal serum and protects carcinoma cells against such serum.

Ishiwara[28] studied the carcinolytic reaction in transplanted rat sarcoma. The normal lytic action disappeared on the thirtieth day after transplantation; lysis began to reappear as the tumors regressed. In 53 tumor cases, Arzt and Kerl[29] found the serum to have no carcinolytic activity in 83 per cent. Twelve and five-tenths per cent. of 16 non-tumor cases reacted in the same way. They compared these results with those obtained by others with the meiostagmin reaction. Of 399 tumors cases, 83 per cent. gave a positive meiostagmin reaction; 548 non-tumor cases gave 9.5 per cent. of positive reactions. Frankenthal[30] criticized the Freund-Kaminer reaction upon the ground that it had never been established whether the lysis of carcinoma cells in normal serum is a specific action or a non-specific autolytic phenomenon which might occur in any serum. She concluded, after trial, that the reaction is not constant or specific and that it has no diagnostic value. Koritschoner and Morgenstern[31] tried to improve the technique of the reaction by applying the refractometric method for the determination of an increase in soluble protein. Of 50 persons free of carcinoma and fever, 47 gave increased refraction after action of the serum on prepared carcinoma cells, indicating lysis of the cells. Of 38 inoperable carcinomas, 37 showed no change or a lowering of the refractive index.

From the above and other reported results obtained with the Freund-Kaminer reaction it is fair to conclude that in about 85 per cent. of cases the serum of cancer patients does not dissolve carcinoma cells, that about 15 per cent. of individuals free of tumor react in the same way, and that the reaction is an interesting but not specific one.

Hemolysis.—Kelling,[32] in 1906, discovered that the blood serum of cancer patients has the property of dissolving the red blood corpuscles of human beings and of certain species of lower animals. The hemolytic action was constant and was not dependent upon nutritional conditions. It disappeared following radical removal of the tumor, but reappeared after recurrence. He claimed that a similar hemolytic property developed in the blood of animals following injection of tumor tissue. Crile[33] determined the occurrence of hemolysis in a large number of cases, with the following results:

	Number of Cases	Per cent. with Hemolysis
Normal	211	0
Pyogenic infection	71	10
Benign tumors	55	0
Cancer	153	85
Post-operative cancer with recurrence	11	100
Post-operative cancer without recurrence	37	0
Tuberculosis	52	92

Most of the cancer cases of this series with a negative reaction were advanced and inoperable. Crile concluded that the hemolysis test is not a specific carcinoma reaction, but that it yields additional clinical evidence of the presence of the disease. Janeway,[34] who criticized the technique used by Crile, obtained only 40 per cent. of positive hemolytic reactions in 20 cases of late malignant disease and 57 per cent. in seven early cases. Ottenberg and Epstein[35] had 76 per cent. of positive reactions in 38 cases of malignant disease, 50 per cent. positive in 40 cases of other diseases, and one positive in 22 normals. They believed that both the varying hemolytic titer of the serum and the varying resistance of the corpuscles used had to be taken into consideration in estimating the results of the hemolytic reaction; they concluded that hemolysis was not to be relied upon for the diagnosis of cancer. By a later modification of his original technique, which consisted merely in diluting the serum 1:10 and incubating for 24 hours at body temperature, Kelling[36] claimed to obtain hemolysis with practically 100 per cent. of cancer serums.

Goldberger[37] determined that the erythrocytes of cancer paitents are less resistant than normal corpuscles to hemolysis by lactic and oleic acids. This was not a specific property, since it occurred also in tuberculosis. But the serum of a person with carcinoma protected the red cells against such acid hemolysis to a greater degree than did normal serum. This protective action of cancer serum Goldberger claimed to be specific for carcinoma and he made it the basis of a diagnostic reaction. Sweek and Fleisher[38] could not substantiate this claim. They found no difference in the anti-hemolytic power of normal and cancer serum against acid hemolysis in 18 cases of carcinoma and 12 normals.

Elsberg, Neuhof and Geist[39] introduced an *in vivo* modification of the hemolysis test by injecting subcutaneously five minims of a 20 per cent. suspension of washed, normal, human erythrocytes. In patients with carcinoma a hemolytic discoloration of the skin made its appearance about five hours after the injection and reached its maximum in six to eight hours. They found the hemolytic reaction positive by this method in 90 per cent. of patients with carcinoma, and negative in 94 per cent. of controls free of cancer. Gorham and Lisser[40] believed that the results obtained by Elsberg, Neuhof and Geist might be due in part to the normal isohemolysins of human blood. They therefore repeated the work, using the four groups of human corpuscles and found that only Group IV (Moss; Group I, Jansky) corpuscles should be used. Even with this modification they did not consider hemolysis specific for carcinoma; the reaction was positive in 60 per cent. of carcinoma cases and negative in 89 per cent. of normals. They could establish no connection between a positive skin test and test tube hemolysis. Lisser and Bloomfield[41] tried the method, using only Group IV corpuscles, in a further series of cases. Two-thirds of the cancer cases were positive. Of the controls, 91.6 per cent. gave a negative reaction and 8.4 per cent. a positive reaction. They concluded that a negative result had little value, but that a positive reaction was strong presumptive evidence of carcinoma.

Farmachidis[42] devised a cobra venom-hemolysis reaction which he believed to be specific in carcinoma. He found that cancer serum caused hemolysis of rabbit erythrocytes in the presence of cobra venom, in dilutions of the latter which alone would not hemolyze the corpuscles. He looked upon the reaction as an activation of a hemolysin present in the serum of cancer patients. Hemolysis did not occur in the presence of normal serum, and sarcoma serum had an anti-hemolytic action stronger than that of normal serum. In a later report upon the method he[43] claimed that the reaction was immediately positive in 53 of 64 cases of carcinoma and appeared later in the remaining 11; it was negative in all of 62 benign tumors.

The search for a hemolytic reaction has appeared to have a basis in the fact that extracts of tumor tissue may be hemolytic. Kullmann,[44] Micheli and Donati,[45] San Pietro[46] and others prepared extracts of carcinoma tissue which dissolved the red corpuscles of human blood and of the blood of different species of lower animals. Weil[47] showed that the hemolytic activity of tumor extracts varies with the amount of necrosis present in the tumor, although the dialysable hemolytic substances of tumor extracts appeared to differ from those which can be obtained from autolyzing normal tissues. Hemolysis is not common to all tumors, and it does not appear to be due to products formed by the metabolism of living tumor cells, but to products of tumor tissue disintegration. The hemolytic phenomenon, while thus far not utilizable diagnostically, may be a factor in the anemia of tumor cachexia.

Enzymes of Tumor Tissues.—Dead tumor tissue rapidly undergoes autolysis, both in the body and *in vitro*, indicating the presence of autolyzing enzymes. The optimum hydrogen-ion concentration and the end products of tumor autolysis were found by Falk, Noyes and Sugiura[48] to be similar to those of normal tissue autolysis. The ereptases or proteases of tumors have often been found to be more active than those of normal tissues and tumor tissue may autolyze more rapidly than normal tissue, but the latter may show such degrees of variation in ereptic activity that a mere quantitative difference in activity is not enough to make possible a differentiation of the autolyzing enzymes. Hamburger[49] could detect no qualitative differences in the ereptases of tumors as compared with those of normal tissues, and believed the ereptases from different sources to be identical and to be derived from the fixed tissue cells. In addition to ereptase, most of the other enzymes which may occur in normal tissues, have been found to be present in tumors. Buxton and Shaffer[50] reported the presence of amylase, glycogen and sugar splitting enzymes, lipase, rennin, catalase, oxidase, and peroxidase; the enzymes were present in larger amounts than in embryonic tissues. Menten[51] obtained a more marked oxidase reaction in tumors when degenerative changes were present. Rosenthal[52] found no noteworthy difference in the catalase content of the liver of normal and carcinomatous mice. But after the intraperitoneal injection of tumor tissue into normal mice the catalase content of both the liver and blood was reduced to about one-fifth of its original activity; this effect was believed to be due to a ferment poisoning action of the disintegrating material. The enzymes capable of acting upon nuclear derivatives are present as in normal tissue. Long[53] found the purine enzymes to be in general the same as in the corresponding normal tissue. Since xanthine oxidase is one of the last of the purine enzymes to develop in the fetal organism, he held that the absence of this ferment in a tumor is evidence of its embryonal character. Tumors of organs which form specific ferments, as the gastric mucosa and pancreas, may continue to form the characteristic enzymes. Ordway and Kellert[54] could detect no change in the complement content of the blood in malignant disease. Dick,[55] on the other hand.

claimed that the complement is increased, varying from one to five times the normal in ten cases of cancer.

Antitryptic Reaction.—The antitryptic action of the blood of cancer patients may be much greater than normal. Brieger and Trebing[56] claimed that the antitryptic activity is increased even before cachexia develops, and that the determination of the antitryptic titer may be a diagnostic aid. Salomon[24] believed the increase to be due to antiferments formed against the trypsin of tumor tissue. Roche[57] found the antitryptic titer of the serum increased in 77.3 per cent. of 22 cases of malignant disease and in 20 per cent. of cases free of tumor. Braunstein[58] believed that an increased index in a doubtful neoplasm, in the absence of complicating factors like tuberculosis, was in favor of a diagnosis of malignancy. Increased antitryptic activity of the blood serum occurs in cachexia in general, and in diseases, other than malignancy, in which there is leukocytosis or destruction of tissue. Weil[59] said that increased activity was of little diagnostic value because it occurs in so many conditions other than neoplasia; a low index might be of some value in excluding cancer.

Protective Ferment Reaction.—Abderhalden's[60] conception, that proteins not identical with the normal ones of the body lead to the development of a protective mechanism characterized by the formation of specific proteolytic ferments whose function is the destruction of the abnormal protein, was early applied to cancer for diagnostic purposes. The presence of such ferments in the blood was detected by permitting the blood serum to act upon a blood-free substrate made from the tissue in question; the occurrence of protein cleavage products in the dialysate was determined by means of the qualitative ninhydrin color reaction. Applied to the serum of suspected cases of cancer, using prepared carcinoma tissue as substrate, the Abderhalden test soon led to a large amount of work and to a voluminous literature. Everyone emphasized the extreme technical difficulty of the method, which interfered with its clinical use and was apt to yield false results. The enthusiasts claimed that the test was so specific that it would differentiate between carcinoma and sarcoma, and that it would even permit a differentiation of carcinomas arising in different organs. The accumulation of data, however, soon indicated a wide divergence of opinion, the extremes of which are illustrated by the reports of Frank and Heimann[61] and of Celler and Stephan.[62] Frank and Heimann obtained positive results in 53 of 54 cases of carcinoma and negative results in 19 of 20 normal serums. Celler and Stephan, on the other hand, claimed that the reaction is of no great value in tumor diagnosis because of the frequent occurrence of non-specific reactions. As a result of their experience they maintained that tumor tissue as such does not cause the formation of protective ferments; the latter appear only, if at all, after the autolysis of tumor tissue and the resorption of split products by the blood. Schumkowa-Trubina,[63] although accepting the protective ferment concept, claimed that the Abderhalden test was not specific for cancer. This conclusion was based upon the fact that the serums of 50 of 73 carcinoma cases gave positive results with placental tissue, and of normal gravidæ 13 gave positve reactions with carcinoma substrate. This writer collected from the previous literature the results of 927 tests of which 635 were considered specific by the 18 investigators who reported them; in 292, reported by two workers, the results were less satisfactory. These results may be tabulated as follows:

	Total	Postive	Negative	Doubtful
I. Results satisfactory:				
Carcinoma cases	424	403(95%)	20(5%)	1
Cases other than carcinoma	211	20(9%)	189(90%)	2
Total	635			
II. Results unsatisfactory:				
Carcinoma cases	142	43(30%)	99(70%)	
Cases other than carcinoma	150	30(20%)	120(80%)	
Total	292			

The discordant results obtained led to attempts at improving the test by the introduction of quantitative methods for the estimation of the degree of proteolysis occurring in the serum-substrate mixture. Dick[55] used the formol titration method for amino-acids; he found no constant variations in cancer serum as compared with normal serum. Lowy[64] applied the Van Slyke method for amino nitrogen. By this method 83.3 per cent. of 42 cases of carcinoma were held to give positive results, and 85 per cent. of 40 non-malignant cases gave negative results. Levin and Van Slyke[65] also used this method, but with results quite different from those obtained by Lowy. They found that the increase of amino nitrogen covered as wide a range in normal serums as in those from carcinoma.

Comparison of Diagnostic Reactions.—A number of investigators have made comparative tests of two or more of the proposed diagnostic reactions. Burmeister[9] compared the meiostagmin and epiphanin reactions, and found neither of value. Coca[13] found both the Freund-Kaminer cytolytic reaction and the v. Dungern complement fixation reaction unreliable. Hara[66] considered the meiostagmin reaction fairly useful and complement fixation more specific, and believed that while the two methods do not give identical results they supplement each other. Brüggemann[67] obtained positive hemolytic reactions in only 51 per cent. of 78 malignant tumors, but considered the meiostagmin reaction useful. Halpern[68] held the Kelling hemolytic reaction and the Freund-Kaminer carcinolytic reactions to be of little value; the only reactions which he considered possibly useful, but requiring more confirmation, were the meiostagmin, complement fixation and Abderhalden ferment reactions. In 35 cases of carcinoma Mioni[69] obtained 57 per cent. of positive meiostagmin reactions, 62 per cent. of positive hemolytic reactions, 11 per cent. of positive hemolytic reactions by the *in vivo* method of Elsberg, Neuhof and Geist, and a characteristically high antitryptic index in 91 per cent. Complement fixation he found unreliable, and passive anaphylaxis uncertain. A report which represents a surprising amount of work, carried out over a period of six years on a large number of tumors, is that of Wolfsohn[70]. He tried the following reactions: Precipitin, hemolysis (in its various modifications), complement fixation, anaphylaxis, cytolysis, Abderhalden ferment, antitryptic index, epiphanin, meiostagmin, and erythrocyte resistance. From his results, which are given in a series of tabulations, he reached the conclusion that a diagnostic cancer reaction to be of value should be clinically specific. Most of the proposed reactions were not specific in this sense and were, therefore, of little practical value. Certain of the reactions, like the meiostagmin and the Abderhalden, might be considered specific in a biologic sense, but had little clinical application because of their technical difficulty.

A review of the various proposed diagnostic tumor reactions leads to the conclusion that none is specific. All have brought to light interesting phenomena, and the positive results obtained by some may have a limited degree of confirmatory value. The literature of the diagnostic cancer reactions is interesting chiefly because it illustrates a peculiar mental reaction, which is equally apparent in the cancer cure and the cancer parasite literature. In each of these fields there is evident, following every supposed discovery of something new, a gullibility which can be explained only upon the basis of loss of calm judgment due to a too enthusiastic immediate acceptance of something acclaimed as an epoch-making discovery. Only with the passage of time and with a more critical evaluation of the data obtained does the new discovery take its proper place as a modest, but by no means epochal addition to the sum total of human knowledge.

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IMMUNITY IN CANCER

What has been said above in regard to the fulity of antibody reactions as a basis for diagnostic tests for cancer has some bearing upon the question of immunity in tumors. That human beings differ in their susceptibility or resistance to neoplasia is apparent from the variations in tumor incidence with which all are familiar. But no insight into the factors concerned in these differences was obtained until the discovery of the transplantability of certain tumors of lower animals. It can not be claimed that such research has given us any great store of positive knowledge, but it has shown that the immunity of the tumor investigator is something different from the immunity of the bacteriologist. The absence of detectable specific antibodies indicates not merely the close relationship of neoplastic and normal tissues, but also that those humoral immune phenomena with which bacteriology has acquainted us are not widely or at all applicable in explaining tumor resistance.

Cytolysis.—Cytolytic activity of the body fluids against cells, whether the latter come from normal tissues or from tumors, is probably a normal mechanism which may, in fact, explain resistance to cancer. But that the human body ever develops specific immune bodies, of protective value against tumors, appears doubtful. If we must suppose that such antibodies are formed, the practically constant victory of malignant tumors over their hosts would indicate that the tumor forms protective antibodies against the body mechanisms, rather than the other way about.

Acquired Resistance.—The experimental researches of Clowes,[1] Clowes and Baeslack,[2] Ehrlich,[3] Michaelis,[4] and Borrel[5] during the years 1905 to 1907, and of a host of other investigators who have followed them, have established that spontaneous regression of a transplanted tumor renders the animal insusceptible to a second transplantation, and that inoculation of a mass of tumor tissue without an actual "take" may have a similar effect. That this increased acquired resistance to tumor is not due to specific antibodies was indicated by the work of Schöne,[6] Borrel,[5] Bridré,[7] Moreschi,[8] Apolant,[9] Bashford, Murray and Haaland[10] and others, who brought about a similar refractory condition by the use of various normal adult and embryonic tissues. That the implanted normal tissue need not be derived from another animal of the same species was shown by Woglom,[11] who caused the development of a tumor resistant condition in mice by removal of the spleen and implantation of the organ into the animal from which it had been removed.

Athreptic Immunity.—While it has been possible, by these procedures, so to increase the resistance of an animal that transplantation becomes unsuccessful, similar methods have not, in general availed to bring about the regression or disappearance of already established tumors. Since it was impossible to adduce evidence that such an acquired resistance is due to specific antibodies, Ehrlich[3] brought forward his theory of athreptic immunity. He believed that tumors require some specific substance which acts as a stimulus to the metabolism of the tumor. If this hypothetical *x*-substance is naturally absent, the animal is naturally resistant to tumor. If the animal acquires resistance as the result of such experimental procedures as have been described above, Ehrlich supposed that the necessary substance had been exhausted by the immunizing material. Against this ingenious theory may be urged that a progressively growing, malignant tumor never exhausts this material, and that a second transplant may often be successful in an animal with a well-developed tumor.

Tissue Reactions.—Local tissue reactions, developed or stimulated as the result of the absorption of inoculated tumor or normal tissues, would appear to be more important agencies in this acquired resistance than humoral antibodies or athrepsia. A greater degree of inflammatory reaction about the transplanted tumor graft in resistant animals was described by Clowes[1] and by Burgess.[12] The latter ascribed the chief rôle in bringing about disappearance of the graft to the new formed connective tissue elements, which produced a zone of fibrous tissue that interfered with the nutrition of the implant. V. Dungern and Coca,[13] who worked with a transplantable sarcoma of the rabbit, believed the refractory condition to be due to a local anaphylactic reaction, resulting from sensitization of the animal's tissues by the immunizing inoculation. Others have sought the explanation of the phenomenon, not in the fixed tissues but in the emigration of lymphocytes into the tissues about the implant. De Fano[14] laid greatest stress upon the plasma cells and considered their presence about transplanted tumors of immune animals an evidence of participation of the body as a whole in the refractory condition. He believed that the lymphocytes also take an important part in the local reaction. Apolant[15] claimed that removal of the spleen prevented or retarded the development of a refractory condition to transplanted tumor. Murphy[46] found that the early chick embryo has no defensive mechanism against implanted tissue, and that it was possible to make successful inoculations and carry on continued propagation of rat sarcoma in such embryos. He[17] next showed that the chick develops defensive mechanisms at about the time of hatching, when the lymphoid tissues become active, and that a refractory condition could be brought about in earlier embryos by implantation of adult chicken spleen or bone marrow. In later work Murphy and Taylor[18] attempted to show that the lymphocyte is also the chief factor in tumor resistance in mice, by preventing the lymphocytic response by means of roentgen radiation, which causes a disappearance of the lymphocytes. Although Murphy's work on the chick embryo was most striking and suggestive, his later results in mice have not been confirmed by Sittenfield[19] and Prime.[20]

Immunity does not appear to be the proper word to apply to the refractory condition which may be experimentally produced in animals. Woglom[21] even doubts that there is an actual increase in resistance, or that the phenomena occurring in and about regressing tumors are essentially different, either qualitatively or quantitatively, from those which occur in and about actively growing ones.

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GENESIS OF TUMORS

The actual genesis of tumor formation is unknown. It is therefore possible to discuss only certain accessory factors which appear to play a part in neoplasia.

Tissue Misplacement.—Embryonic misplacement of tissue no longer has the universal application to the origin of tumors that Conheim[1] postulated for it. The occurrence of misplacement is not, however, to be doubted, the proof being furnished by those malformations which are best explained upon a misplacement basis; by the teratomatous and mixed tumors, which may manifest their presence either in childhood or not until later in life; and by the small islands of normally differentiated, non-blastomatous salivary gland tissue found in regions of the face and head where they should not occur, pancreatic tissue seen not infrequently in the wall of the gastrointestinal tract, and adrenal tissue encountered along the entire course of the urogenital tract. The process occurs probably much more frequently than the illustrations given indicate. The discovery at necropsy of bits of misplaced tissue is often a matter of chance; probably many more examples go unrecognized than are found. That misplacement should occur during the complicated processes of embryogenesis and organogenesis is not so great a matter for surprise, as is the fact that a certain, perhaps only small number of such misplacements, should apparently go on to the formation of the progressively growing tissue aggregates which we call tumors. The phenomenon of misplacement seems to be a much more important element in the tumors of childhood, especially those which may be considered congenital in origin even if, as in the case of certain dermoids and teratomas, they are not discovered until later in life, than in the usual blastomas of the adult period. That a relationship exists between misplacement of tissue and the development of many of the tumors of childhood must be granted, but what there is in this relationship which should lead to the acquisition upon the part of the misplaced tissues of unlimited and uncontrolled proliferative activity is unknown. The mere fact of misplacement is not sufficient explanation, since the number of masses of misplaced tissue which reach a condition of complete differentiation and of equilibrium with the tissues in which they are embedded is probably vastly greater than those which form tumors.

Misplacement may occur at any period of embryonic development. The stage at which it occurs appears to be important in determining the nature of the tumor which may result. Occurring early enough, a separated blastomere may give rise to a complete, normal embryo. Occurring somewhat later in this early stage, the misplaced blastomere, still with totipotent qualities, may give rise to a complicated teratoma. Occurring still later, cells of pluripotent qualities may give rise to teratoid or mixed tumors. But misplacement need not be a complete dislocation of cells from their normal situations. A group of cells within a developing organ may fail to establish normal relations with the rest of the organ; their location is normal, but they are misplaced in the physiologic sense, a condition which appears to lead to an inhibition (or *Hemmung*) of further normal development. Such islands of tissue may form adenomas or other homoglous benign tumors in organs which are the normal site for the tissue. From such benign maldevelopments malignant neoplasms may apparently arise at any period of life. Here again there is an unknown factor which permits such a benign adenoma, for instance, to lie dormant throughout the life of the individual in one case, and causes it to go on to the formation of a highly malignant carcinoma in another.

Hamartoma.—Choristoma.—Dislocation of cells during embryogenesis is probably the result of mechanical factors. During recent years there have been developed several conceptions other than actual dislocation which will theoretically explain the presence of a mass of tissue in a situation where it should not occur. Albrecht[2] separated out from the group of abnormalities previously considered the result of misplacement those which he conceived to be due to overdevelopment of some tissue element, which belongs normally at the site where it is found, and those due to abnormal relationships of normally situated tissue elements. To such abnormalities he applied the term hamartoma, and gave as examples the not infrequent small adenomas and adenofibromas of the kidney, fibroadenoma of the mammary gland, leiomyoma, and agnioma. For certain true misplacements, that is, tissue aggregates found in situations where they do not belong, Albrecht postulated an origin from embryonic tissues of pluripotent qualities. Thus, he conceived that the entire anlage of the midgut has the potientiality of forming pancreatic tissue. Pancreatic misplacements, according to this conception, need not, therefore, be the result of actual dislocation or transplantation of embryonic pancreas, but could arise *in situ* as the result of local differentiation of midgut tissues to pancreatic tissue. To abnormalities of this type Albrecht applied the name choristoma.

Progonoma.—In 1922, Mathias[3] introduced still another conception and still another term, namely, progonoma. He considered the resultant misplacement to be due to fetal atavitism, to the occurrence in the ontogeny of the individual of phylogenetic stages which do not normally occur in the life history of the species, but do occur in ancestral forms of the species. Thus, he explained pancreatic misplacement by the formation of multiple pancreas anlagen, a process which does not occur normally in the human embryo, but is a normal phenomenon in the development of teleost fishes. The frequent salivary gland misplacements he explained as the result of a similar process.

The conceptions of Albrecht and Mathias, which have led to the introduction of new names for old things, are not susceptible of proof. They are nevertheless valuable because they give us additional and reasonable hypotheses to explain so important a biologic phenomenon as tissue misplacement. They do not explain the acquisition of autonomous growth by the hamartoma or choristoma or progonoma, even if we grant that the postulated processes play a part in the formation of the latter.

Heredity.—The occurrence of cancer in several adult members of a family is suggestive of the working of an hereditary factor, and many family lines with an undue incidence of carcinoma have been reported as evidence of the influence of such a factor. Such data are often of little value because most human genetic records are incomplete, both in respect to any knowledge whatever of the collateral lines and in respect to information of the exact cause of death of even the immediate ancestors in the direct line. Levin,[4] who criticized previous studies of tumor families because they did not take into consideration the total members in each generation who reach the cancer age. made an analysis of two families the records of which were complete for six generations. He concluded that resistance to cancer is a dominant character, which is transmitted according to mendelian laws. Absence of this character creates susceptibility. Warthin[5] made a study of the familial occurrence of carcinoma in 1106 cases, in which the diagnosis was established by microscopic examination in his laboratory. His material showed a high susceptibility to carcinoma in certain families and family groups, most striking among which was a family of 48 descendents of a cancerous grandfather with 17 cases of carcinoma, 10 of the uterus and seven of the stomach. The multiple occurrence of cancer in one generation was usually associated with carcinoma in the preceding generation. When both maternal and paternal lines were involved, the tendency to the disease was greatest. Families with carcinoma in several generations showed a decided tendency for the condition to develop at an earlier age and to assume greater malignancy in each succeeding generation. Among the neoplasms of childhood a strong familial tendency is apparent in glioma of the retina and in xeroderma pigmentosum, the latter being characterized by the occurrence of multiple epitheliomas of the skin.

The most important work dealing with the role of heredity in neoplasia is that of Maud Slye,[6] relating to the occurrence of spontaneous tumors in mice. Her animals, whose genetic histories are completely known for many generations and over a period of time which would correspond to several hundreds of years in the human species, are permitted to live out their lives under the best possible conditions and are not subjected to any experimental procedures except selected mating. The cause of death, the occurrence of tumor, and the nature of the latter if present are determined by a complete necropsy of every animal, confirmed by microscopic examination. Slye's work has conclusively proven the importance of heredity in the tumors of mice, since she is able at will to introduce tumor into any family line or to eradicate it from any line by selective breeding. She believes that her work shows that cancer and non-cancer tendencies are unit characters which segregate out and are transmitted as such according to mendelian laws. She looks upon cancer as the absence and non-cancer as the presence of a mechanism which controls proliferation and differentiation. The individual who is normal in so far as neoplasia is concerned would be one to whom this mechanism is transmitted; the abnormal individual, who would be susceptible to tumor, would fail to receive the regulatory mechanism. Given the inherited tendency or susceptibility to tumor formation as the result of the failure of transmission of the mechanism which controls proliferation and differentiation, then any one of a number of accessory factors may act to bring about the development of a neoplasm. Some objection has been made to Slye's work upon the grounds that she has practiced inbreeding and that the data obtained from the study of mice are not directly applicable to human beings. To the first of these objections the answer may be made that inbreeding is not a valid criticism, if by selective inbreeding it is possible not only to transmit the tumor tendency but also to eliminate it entirely and to maintain the inbred line free of tumor for as many generations as may be desired. To the objection that the data obtained from the study of mice can not be applied to man, the answer is to be made that inheritance is a biologic phenomenon which acts apparently in the same mathematically exact manner in every species, whether plant or animal, in which the union of two gametocytes is followed by chromosomal segregation. Not until equally complete human genetic histories over an equal number of generations bring to light facts which can not be reconciled with those which hold for mice, will it be possible to say that the data which relate to the rôle of heredity in the tumors of mice are not directly applicable to human beings.

Inflammation and Injury.—For a small number of neoplasms of adults trauma, and for a larger number chronic inflammation appear to be contributory factors. The occasional association of sarcoma with trauma, and the more frequent association of carcinoma of the stomach, gall-bladder, uterus, mammary gland, and lip with chronic inflammation can not be entirely disregarded. The relationship exists, but how trauma or inflammation acts to cause tumor formation is unknown. The mere initiation of proliferative changes in the tissues does not explain the formation of tumors, since the latter follow only a relatively small number of the injuries and inflammations to which human tissues are subjected. In organs like the uterus and mammary gland, physiologic trauma, if one may apply this term to the succession of alternate stages of hyperplasia with active function and of regression to the resting stage, may be as important as injury or inflammation in the usual sense. But such physiologic changes also occur more frequently without than with tumor formation.

Ribbert[7] modified Cohnheim's misplacement doctrine to make it more widely applicable to the tumors of adults, and especially to those in which chronic inflammation appears to be a factor. He supposed that the latter process causes local displacement of tissue, with a resulting loss of the mutual restraint which normal tissues exercise upon each other. It is conceivable that, in those organs which undergo one or more periods of great physiologic activity followed by regression, the latter process may not run its normal course and may also result in disturbance of the restraint which stroma and parenchyma mutually exercise. But to grant such loss of restraint, either as the result of inflammation or of abnormal regressive changes, merely states an occurrence, and does not establish an actual cause of neoplasia. In the tumors of children, inflammation and injury are much less frequently associated conditions than in those of adults. In a few neoplasms of children, such an association has been emphasized, but the number is quite small.

Parasites.—With the development of bacteriology and protozoology, and with the establishment of the importance of microorganisms in the causation of disease, it was natural that parasites should be sought in tumors as the essential etiologic agents. Many varieties of tumor parasites have been discovered and seriously heralded as causes of tumor formation. But in the published reports of parasitologic investigations of cancer there is apparent such a tendency for individual investigators to permit themselves to be influenced by the prevailing mode in parasites, that one views each new tumor parasite with skepticism. The cancer literature reveals a series of cycles in which protozoan parasites, described as amebæ, coccidia, myxosporidia, etc., were succeeded by blastomycetes, and these in turn by spirochetes. Now and then an investigator who has lived through more than one such cycle has been able to alter his convictions in regard to his own cancer parasites as the style changed; following Sanfelice his cancer parasite was a blastomycete, and following Schaudinn it was a spirochete. Bacterial parasites, sometimes coccoid and somestimes bacillary, have been repeatedly observed, cultivated, and made to yield curative serums. That living organisms may be associated with tumor formation is established by the experimental production of epithelioma of the rat's stomach by Spiroptera and by the occurrence of epithelioma of the urinary bladder in Bilharzia infection and of bile-duct carcinoma of the sheep's liver in infestation by the liver fluke. But these are examples of a relation between chronic inflammation and tumor, not of actual causation of tumor by parasites. The transmission of tumor-like conditions by living virus appears to be established for fowl leukemia and for the Rous chicken sarcoma. But the mere fact that these conditions seem actually to be due to a living virus is enough to make one doubt they are true neoplasms. The evidence thus far available does not permit the acceptance of a parasitic etiology of tumor formation.

Sex.—In the post-adolescent tumors, sex is important in determining incidence. In 47,986 deaths due to malignant disease, as tabulated in the Bureau of the Census Report[8] on cancer in 1914, the ratio of females to males was as 60 to 40. The reason for this greater frequency among females becomes apparent at once when the relative incidence of organ involvement is considered. Seventy-three per cent. of this large number of tumors occurred in only five organs, in the following order: Stomach, 24.45 per cent.; uterus, 13.81 per cent.; liver and gall-bladder, 12.47 per cent.; intestine (including rectum and anus), 12.00 per cent.; breast, 10.54 per cent. With the uterus ranking second and the mammary gland fifth in tumor incidence, the greater frequency of malignant tumors as a cause of death in females is explained. In children a sex difference is not so apparent, although certain of the tumors of childhood occur more frequently in one sex than in the other. In Steffen's[9] collection of 789 malignant neoplasms in children, tumors of the intestine, peritoneum, larynx, brain and meninges were more frequent in boys than in girls. Philipp,[10] in his series of 87 carcinomas of childhood, found no difference in the two sexes. Fischer[11] collected 41 examples of the embryonic renal tumor in males associated with tuberous sclerosis of the brain to seventeen in females. Against the greater preponderance of the above tumors in boys must be placed a much higher frequency of tumors of the ovary than of the testis. According to Bossard,[12] hemangioma of the skin is more frequent in girls than in boys.

Age.—Tumor incidence increases steadily with age, to such a degree that advancing age must be considered an important accessory factor in the causation of tumor. Since it is the ageing of the tissues which appears to make them susceptible to neoplasia, the age factor should theoretically be of little importance in the tumors of childhood, except to explain the lower incidence during this period. But as will be shown later, in the more detailed discussion of the incidence of tumor in the early years of life, there is a period of relatively high incidence during the first year of life. This is due to a group of congenital tumors, which lead to death shortly after birth or even *in utero*. Age does not appear to be the real factor in this group; misplacement, maldevelopment, and the unknown factors which lead to tumor formation before birth are more important.

Modern microscopic research and experimental investigation have added much to our knowledge of the characteristics of neoplasms, but have diminished very little or not at all our lack of knowledge of what causes a tumor. This is not said in belittlement of modern tumor research, but in an attempt to evaluate our present store of information and to envisage what still remains for the future to unfold for us. Present-day methods of investigation must be continued and must be multiplied in order to complete our knowledge even of the characteristics of neoplasms. But the tumor problem, the problem of the actual cause of tumor formation, is a problem of abnormal cellular biology. Until our knowledge of what is occurring within the tumor cell itself is vastly greater than it is today, the tumor problem will remain unsolved. Before the solution is reached, and the solution of the tumor problem will probably be the last attainment of biologic research, the biochemist and the biophysicist and the biocytologist will need to increase very materially our present array of data relating to the phenomena which occur in the complex protoplasmic system of the living normal cell.

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INCIDENCE OF TUMORS IN INFANCY AND CHILDHOOD

Relative Age Incidence of Tumors.—An accurate estimate of the frequency of tumors in the early years of life is impossible because of the uncertainties which are inherent in all tumor statistics. The generally accepted belief that tumors are relatively infrequent in childhood as compared with later years of life is borne out by statistics, but the latter do not permit definite prognostication as to the actual number of tumors which may be expected in any juvenile population. Such statistics as we have are based upon collections from clinics or institutes, upon morbidity figures and upon mortality tables.

The tabulations based upon operating-room and post-mortem figures have the advantage of accuracy of diagnosis. They have the disadvatage of giving only the proportion of tumors in children to the total number of tumors which have come to examination. They do not give information as to the actual number of tumors occurring in the early period of life, nor do they give with any degree of exactness the relative frequency as compared with later years. Of the tabulations of this kind, that of Warthin[1] is especially valuable because it is based upon a relatively large number of cases from a single clinic and because the material represents a homogeneous population. In a group of 2000 tumors whose nature and malignancy were determined by microscopic examination, 42 or 2.01 per cent. occurred in children before the age of 15 years. This percentage based upon both surgical and autopsy material is higher than that usually found in a series of post-mortem examinations alone. In 803 necropsies on cases of malignant disease, the tabulations of Nobiling[2] and of v. Mielecki[3] give a total of only five malignant tumors (one carcinoma and four sarcomas) or 0.62 per cent. in persons under 20 years of age.

Morbidity statistics are vitiated by possible errors in diagnosis; furthermore, since cancer as a disease rather than as a cause of death is not reportable, such morbidity figures as have been obtained are usually the result of spasmodic efforts to collect data, and they give an indication of conditions as they exist only at a particular time and in a particular country or locality. Of such tabulations those of Fibiger and Trier[4] for Denmark based upon the number of cases under treatment by physicians upon a given date (April 1, 1908) appear to offer the fewest objections. In a population of 2,650,000, the number of malignant tumor cases was 1135, a rate of 43 per 100,000. In this number there were only six or 0.52 per cent. at the ages up to the fifteenth year (five sarcomas and one carcinoma), and six in the age period of 15 to 19 years (five sarcomas and one carcinoma).

Mortality statistics likewise are subject to a variety of errors but give perhaps a better idea of the prevalence of malignant disease in a population than the figures derived from operative or post-mortem material, or from a census of living cases. This is especially true when a careful attempt is made to verify the reports. Such a collection of statistics is that prepared at the request of the American Society for the Control of Cancer by the United States Bureau of the Census for 1914.[5] The total deaths from cancer and other malignant tumors in the registration area of the United States for the year 1914 were 52,420; of these 451 or 0.86 per cent. occurred at ages up to the fifteenth year. The following table (Table 1) gives the distribution at the various age periods up to the thirtieth year; the distribution for each age period per 1000 tumors of the aggregate; the population of the registration area for the different age periods, and the death rate from malignant tumors per 100,000 of population of the given age periods.

Table 1.—Age Incidence of Tumors up to 30 Years. Registration Area of the United States, 1914

Age	Number of tumors	Distribution per 1000 of aggregate	Population	Tumor death rate per 100,000 of population
Under 1 year	49	0.9	1,341,242	3.7
1 year	42	0.8	1,202,228	3.5
2 years	61	1.2	1,310,794	4.7
3 years	43	0.8	1,295,311	3.3
4 years	42	0.8	1,262,416	3.3
Under 5 years	237	4.5	6,411,991	3.9
5 to 9 years	122	2.3	5,873,325	2.1
10 to 14 years	92	1.8	5,600,632	1.1
Under 15 years	451	8.6	17,885,948	2.5
15 to 19 years	174	3.3	5,755,656	3.0
20 to 24 years	294	5.6	5,946,734	4.9
25 to 29 years	587	11.2	5,521,323	10.6

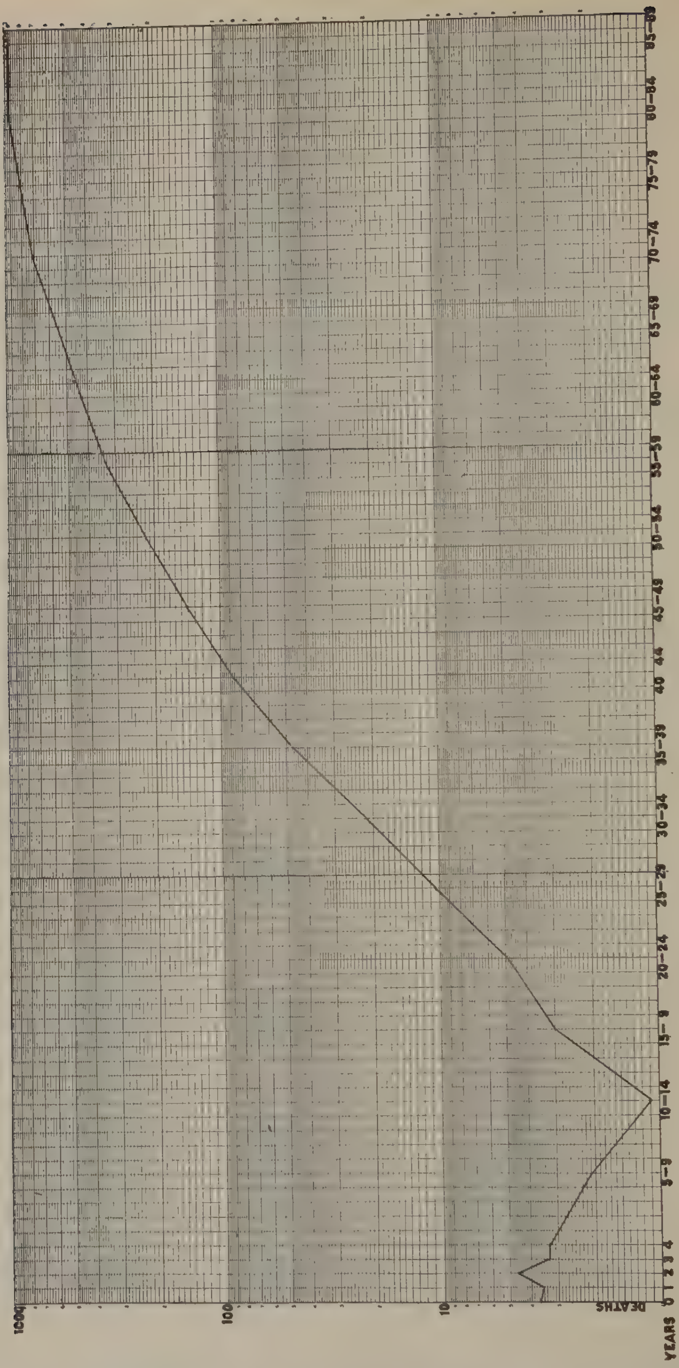

Chart 1.—Age graph of the cancer death rate per 100,000 of population. Based upon 52,420 deaths due to malignant tumor in the registration area of the United States in 1914.

From the 1914 census data we have constructed Chart 1, the graph of the tumor death rate per 100,000 of population at the different age periods. This chart is of especial interest because of the very definite downward course of the curve to the fifteenth year. At this point begins a sharp rise which mounts steadily throughout the later years of life. The break in the course of the curve is undoubtedly due to the deaths early in life caused by the congenital tumors. For the first three successive five-year periods the death rates per 100,000 of population were 3.9, 2.1 and 1.1. The fourth five-year period inaugurates the increasing tumor mortality rate which characterizes adult life. Not until the third decade does the rate again reach the height that it had already attained during the third year of life.

The Relative Frequency of the Kinds of Malignant Tumors. One of the generally accepted dicta of medical lore is that carcinoma is a tumor of later life, sarcoma a tumor of childhood and adolescence. A study of such statistics as are available bears out this belief; but just as sarcoma may arise in later life, so also may carcinoma be encountered early in life. The relative proportion of malignant true epithelial tumors during the first few years after birth is small; unless the tumors are quite characteristic, the diagnosis of carcinoma in infancy must be viewed with skepticism, because of the frequency of mixed tumors which contain atypical epithelial structures.

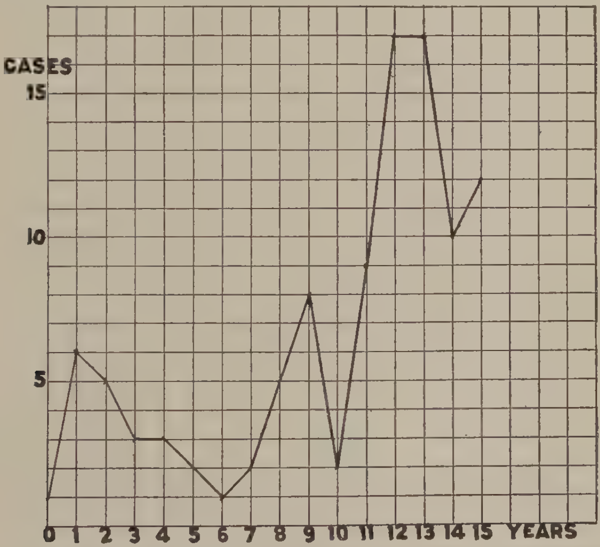

CHART 2.—Age distribution of 104 carcinomas occurring in the first fifteen years of life. (Merkel.[9])

In Williams[6] analysis of 779 malignant tumors, the earliest carcinoma was a columnar cell carcinoma of the rectum at 11 years; he included also a rodent ulcer at 14 years. In Hadda's[7] tabulation, which included 7330 cases of carcinoma at all ages, there were 31 or 0.42 per cent. in the first 15 years of life. Warthin's[1] series included an epithelioma of the ear at four years and one of the skin of the leg at 11 years; an epithelioma of the mouth, a basal cell epithelioma of the eye, an adeno-carcinoma of the stomach, and an adeno-carcinoma of the umbilicus, the latter teratoid in origin, occurred in children aged 14 years; there was one adeno-carcinoma of the ovary at 15 years. This gives six carcinomas in a total of 44 malignant tumors of the first 15 years, a percentage of 13.6. Fibiger and Trier's[4] statistics include a carcinoma of the ileum in a male child aged 3½ years and a carcinoma of the neck, of aberrant thyroid origin, in a girl aged 15 years. In v. Mielicki's[3] 560 necropsy cases of malignant tumor, five occurred before the twentieth year; only one of these was a carcinoma, in a person dying at 17 years of age. To the 37 cases of certain carcinoma during the first 15 years collected by Philipp,[8] Merkel[9] added 17. The age distribution of these 104 carcinomas was as follows: New-born, 1; ¼ year, 1; ½ year, 2; ¾ year, 1; 1 year, 2; 1½ year, 2; 2, 3, 4, and 5 years, each 2; 6 years, 1; 7 years, 2; 8 years, 5; 9 years, 8; 10 years, 2; 11 years, 9; 12, 13 years, each 17; 14 years, 10; 15 years, 12. (Chart 2.)

The relative frequency of sarcoma, carcinoma and mixed or teratoid tumors can not be determined from reported cases, because the mixed tumors are reported by some as carcinoma and by others as sarcoma. Only in a series like that of Warthin,[1] where the microscopic diagnosis of a fairly large number of tumors has been made by the same laboratory, do we find anything of value. In his series of 44 tumors, which occurred in the first 15 years, the distribution was as follows; sarcoma, 31 (70.5 per cent.); mixed tumors, 7 (15.8 per cent.); carcinoma, 6 (13.6 per cent.). A larger series of tumors would probably show a greater proportion of mixed tumors and a lesser proportion of carcinomas.

Benign tumors are very much more frequent than malignant ones. Usener[10] analyzed 173 tumors of children which came under observation at the children's hospital of Leipzig in the years 1907 and 1908. One hundred and sixty-nine, which were benign, fell into the following groups: Hemangioma and lymphangioma, 145; lipoma, 11; teratoma, 8; osteoma, 5. There were only four malignant tumors in the series; all of these were sarcomas.

The Relative Frequency of Tumors of the Different Organs and Organ Systems.—Owing to the greater proneness of certain organs and organ systems to congenital tumors, especially of the mixed or teratoid variety, the distribution of tumors among the various organs during childhood is quite different from that which obtains in later life. Whereas in adult life the stomach, uterus, and liver (including gall-bladder) lead in the order named, in childhood the kidney, the eye and the bones are most frequently involved. The relative frequency of involvement of the different organs can be determined only from larger compilations based upon reported cases; error in diagnosis is a disturbing factor in such statistics, but is minimized if the number of cases included is great enough.

One of the largest tabulations of the tumors of the early years of life is that of Steffen.[11] The distribution of his tumors, arranged as nearly as possible according to the International List which the Bureau of the Census uses, together with the percentages of the total tumors, is as follows (Table 2):

TABLE 2.—ORGAN DISTRIBUTION OF TUMORS IN STEFFEN'S COMPILATION

Organ	Total tumors	Percentage
Buccal cavity:	2	0.25
Tongue	2	0.25
Stomach and liver:	47	5.70
Pharynx	3	0.38
Esophagus	1	0.12
Stomach	4	0.50
Liver and gall-bladder	39	4.94
Peritoneum, intestines and rectum:	31	3.92
Mesentery and peritoneum	10	1.26
Intestines	21	2.66
Female genital organs:	34	4.31
Ovary and fallopian tube	9	1.14
Uterus	5	0.63
Vagina and vulva	20	2.52
Breast	2	0.25
Skin (and soft parts)	53	6.70
Other organs:		
Larynx	14	1.77
Lung and pleura	21	2.66
Pancreas	5	0.63
Kidneys and suprarenals	224	28.39
Prostate	6	0.76
Bladder	32	4.05
Brain and meninges	83	10.52
Testes	13	1.64
Spleen	2	0.25
Bones	71	8.99
Eye and orbit	90	11.41
Heart	2	0.25
Thyroid	3	0.38
Lymph nodes	13	1.64
Thymus	2	0.25
Spinal cord and nerves	9	1.14
Sarcomatosis and carcinomatosis	7	0.88

In Table 3 is given the organ distribution of the tumors reported as causes of death in 1914 in the registration states of the United States.[5] The number of tumors at ages up to 15 years was 413, constituting 0.86 per cent. of the total number of all tumors at all ages of the same population. This table gives, in the first column, the total tumors at all ages for the various organs, as classified by the International List; in the second column, the percentage of total tumors at all ages occurring in the various organs; in the third column, the total tumors per organ at ages up to 15 years; in the fourth column, the percentile organ distribution of the tumors at ages to 15 years; and in the fifth column, the percentage proportion of all tumors of each organ occurring up to 15 years. It is to be regretted that the census statistics do not list separately the tumors of the eye and orbit, which constitute 11.41 per cent. of the total of Steffen's compilation; in the census tables,

TABLE 3.—ORGAN DISTRIBUTION OF TUMORS, CENSUS STATISTICS OF THE REGISTRATION STATES OF THE UNITED STATES FOR 1914

Organ	1 Total tumors at all ages	2 Per cent. of total tumors	3 Total tumors under 15 years	4 Per cent. of total tumors under 15 years	5 Percentage of all tumors of organ under 15 years
Buccal cavity:	2,086	4.34	21	5.21	1.01
Lip	354	0.73	2	0.48	0.56
Tongue	547	1.14	1	0.24	0.18
Mouth	216	0.45	3	0.72	1.38
Jaw	785	1.63	15	3.64	1.91
Others	184	0.38	0	0.00	0.00
Stomach and liver:	18,285	38.10	41	9.92	0.22
Pharynx	50	0.10	1	0.24	2.00
Esophagus	534	1.11	0	0.00	0.00
Stomach	11,733	24.45	7	1.69	0.06
Liver and gall-bladder	5,968	12.47	33	7.99	0.55
Peritoneum, intestines and rectum	6,234	12.99	46	11.13	0.73
Mesentery and peritoneum	447	0.93	15	3.64	3.35
Intestines (except rectum)	3,768	7.85	26	6.29	0.69
Rectum and anus	1,992	4.15	5	1.21	0.25
Others	27	0.06	0	0.00	0.00
Female genital organs:	7,247	15.10	10	2.42	0.13
Ovary and fallopian tube	406	0.84	4	0.96	0.98
Uterus	6,629	13.81	5	1.21	0.08
Vagina and vulva	170	0.35	0	0.00	0.00
Others	42	0.07	1	0.24	2.38
Breast	5,052	10.54	0	0.00	0.00
Skin	1,838	3.83	23	5.56	1.25
Other organs:	7,244	15.09	272	65.85	3.75
Larynx	318	0.66	4	0.96	1.25
Lung and pleura	333	0.69	7	1.69	2.10
Pancreas	617	1.28	2	0.48	0.32
Kidneys and suprarenals	467	0.97	76	18.40	16.27
Prostate	716	1.49	0	0.00	0.00
Bladder	915	1.90	3	0.72	0.32
Brain	123	0.25	7	1.69	5.69
Bones (except jaw)	448	0.93	43	10.41	9.59
Testes	111	0.23	5	1.21	4.50
Others	3,196	6.68	125	30.26	3.91
	47,986		413		0.86

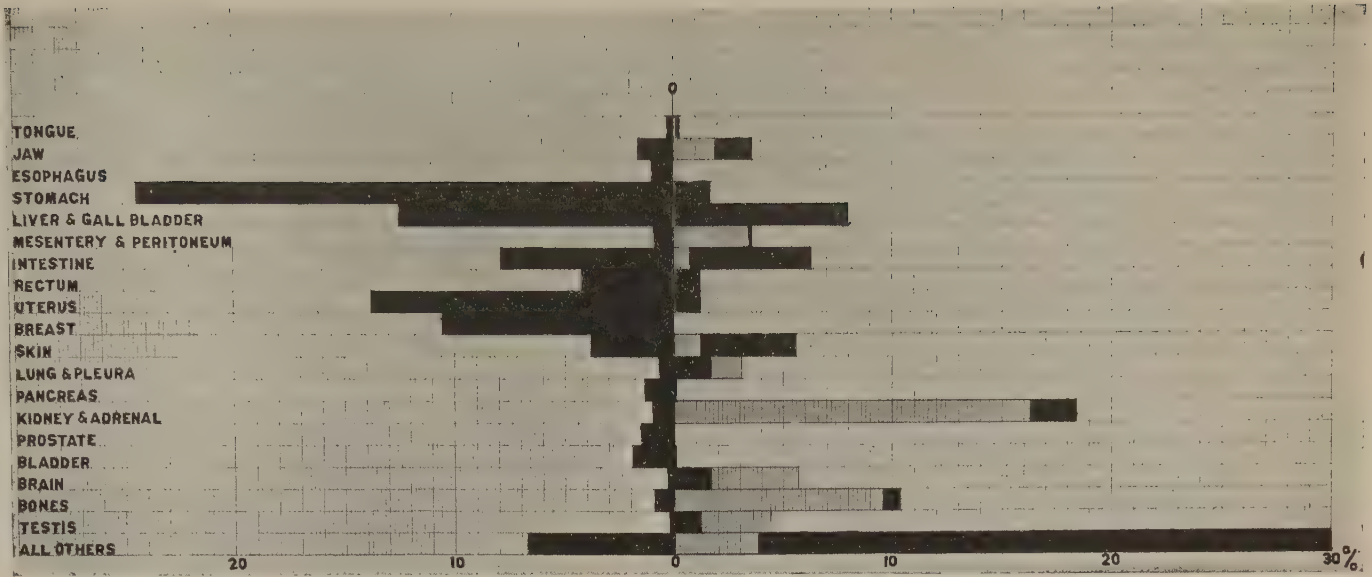

CHART 3.—Relative organ distribution of tumors. Based upon 47,986 deaths due to malignant tumor in the registration states of the United States in 1914. To the left of the vertical zero line is the percentage organ distribution of all tumors at all ages (data of Column 2, Table 3). To the right of the vertical zero line is the percentage organ distribution of the tumors at ages up to 15 years (data of Column 4, Table 3). The shaded portion to the right of the vertical line gives, for each organ, the percentage of all tumors of the organ which fall in the juvenile period (data of Column 5, Table 3).

these tumors are included in the rubric "others" under "Other organs not specified." This "catch-all" group of the census tables includes 125 cases or 30.26 per cent. of all the tumors occurring under 15 years of age. From Table 3 Chart 3 has been constructed.

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CLASSIFICATION

Bland-Sutton[1] in his "Tumours Innocent and Malignant" says: "It may be stated, without fear of contradiction, that no one has succeeded in framing a satisfactory classification." Classification, upon which terminology depends, would be a simple matter if it could be based upon some definite, underlying principle universally applicable to all tumors. But our knowledge of tumors, rich as it may be, has not yet given us such a universally applicable principle. Hence tumors have been classified and named according to some attribute which in the mind of the individual writer was most widely and easily applicable.

Morphologic Classification.—One characteristic of tumors, which is most widely and readily applied, is their structure or composition as determined by microscopic study, that is, their histology or perhaps better, their morphology. The result is that most of the attempted tumor classifications are primarily morphologic. If the examination of a tumor shows it to be composed of tissue not readily to be distinguished from fibrous tissue, for instance, we can add the suffix -oma, meaning tumor, to the root indicating the type of tissue. Thus we arrive at fibroma, and have not merely given a name to a particular tumor, but have indicated its nature and its position in a system of classification.

Such a scheme groups neoplasms according to the normal tissues which the tumor tissues most closely resemble. If it were possible in every case to determine, from the morphology of the tumor, the kind of tissue which composes the latter, then the morphologic classification would be simple. However, it is just in that group of tumors which is most important clinically, the malignant tumors, that the morphologic classification fails. In these, the tissues may be so young and undifferentiated that they have no morphologic identity with any of the normal tissues, and it is impossible to determine the variety of the tumor cell from its appearance. While the purely morphologic classification is, therefore, unsatisfactory, because it fails us in many instances and because it groups together, upon the basis of morphology, certain tumors which have no relationships in their origin, it has given us the great bulk of the names which are still applied to tumors. Any other classification must retain these names, in so far as possible.

Embryogenetic Classification.—Since what we would like to know most about a tumor is its origin, a classification based upon origin rather than upon morphology would be the ideal one. Such a scheme, carried to its logical conclusion, would carry the origin back to the three primitive embryonic germ layers and would classify tumors according to their derivation from these layers. Such an embryogenetic classification was, in fact, attempted by Waldeyer. A difficulty which arises is that it encounters an objection already noted in the morphologic classification, but of different degree. The latter assembles tumors of similar morphology but of diverse origin. The former assembles tumors of diverse morphology but of similar origin. Thus, the glioma, morphologically sarcoma-like, would be placed with a distinctly alveolar epithelioma, because both are derived from the epiblast. Similarly, the markedly glandular tumors arising from derivatives of the middle germ layer would be included in a group with the sarcomatous tumors of mesoblastic origin. Glandular intestinal carcinoma and non-glandular chordoma, both of hypoblastic origin, would find themselves side by side in a third group. A second and insurmountable difficulty is that it is not always possible to determine the origin of a tumor by means of the methods at present available. This latter difficulty, however, applies to all classifications, which take the origin of the tumor into account. If the derivation of a given tumor remains undetermined, then the basic principle underlying the embryogenetic scheme of classification fails.

Histogenetic Classification.—If, instead of attempting to carry the origin of tumors back quite to the primitive germ layers with their undifferentiated cells, we carry the derivation back only so far as the stage of early tissue differentiation, we overcome some of the objections which have been made to both the morphologic and the embryogenetic classifications. At the stage of development when tissue differentiation begins, there are already impressed upon the cells tendencies which manifest themselves later both in the relationships of the tissue constituents to each other and in the morphology of the cells. These tendencies are retained in most tumors, even when the latter are composed of undifferentiated elements. The histogenetic classification is a compromise between the morphologic and the embryogenetic. Of the former, it uses the important element of relationship of the cells to each other; of the latter, it retains the element of derivation of the tumor cells from incompletely differentiated elements. Of the many tumor classifications which have been proposed, that of Adami,[2] a histogenetic classification, appears to present fewest objections and to be philosophically the soundest.

Mixed Tumors.—Before giving Adami's classification it is necessary to discuss certain features which are of extreme importance in the tumors of the early years of life and which influence any classification. Teratology, the study of anatomic maldevelopments, has taught us that the latter may arise by the fusion, during the beginning of embryonic development, of two embryos, or by the separation, at the same early stage of development, of a group of totipotent or pluripotent cells from what was originally a single fertilized ovum. The result of either process, following the varying grades of subsequent development which may occur, may be anything from a misplaced group of cells to a normally formed twin. Of prime importance in the consideration of tumors is the fact that there may result tumors of mixed composition, which cannot be placed in any classification which is based upon tumors whose cells are descended directly from the unipotential cells of the individual. It is, therefore, necessary to make a primary division into tumors of a mixed character and into the autochthonous blastomas. In this primary classification we shall also follow Adami,[2] who makes the following main groups.

I. Teratoma. Tumors derived from cells capable of giving rise to all the tissues of the individual (totipotential cells).
  1. Twin teratoma (geminal or heterochthonous). Example: Fetal inclusion.
  2. Filial teratoma (or autochthonous), due to segregation and subsequent growth of totipotential cells of the individual.
    (1) From non-germinal blastomeres.
      Example: Epignathus, congenital sacral teratoma.
    (2) From germinal cells.
      (*a*) From aberrant germinal blastomeres.
        Example: Sporadic teratoma of cranium, etc.
      (*b*) From unreduced ovarian and testicular germ cells.
        Example: Ovarian and testicular teratomas. Members of this second class may be:
        i. Complete, exhibiting derivatives of all three germ layers, or
        ii. Reduced, derivatives of one germ layer failing to develop.
        They may also be (i) typical or (ii) atypical.

II. Teratoblastoma. Tumors (autochthonous) derived from pluripotential cells of the individual; mixed tumors.
  1. Diphyllic, containing derivatives of two germinal layers.
    Example: Certain parotid and renal mixed tumors.
  2. Monophyllic, containing derivatives from one germinal layer.
    Example: Most renal mixed tumors.

III. Blastoma. Tumors derived from unipotential cells.
  1. Heterochthonous or teratogenic, the cells being derived from another individual.
    Examples: Destructive placental mole and chorio-epithelioma malignum; epithelioma derived from an ovarian dermoid.
  2. Autochthonous, from the independent growth of unipotential cells of the host individual.
    Examples: All other tumors composed of cells of one order.

Autochthonous Blastomas.—Adami's[2] classification of the tumors arising from the unipotential cells of the host individual is based upon his conception of the early tissue differentiation which occurs in each of the three primitive germ layers. From each layer there are formed tissue aggregates which are characterized by the fact that their constituent cells are in direct apposition with each other and are not separated by blood vessels, lymph spaces or supporting tissues; and other tissue groups whose cells are separated by supporting matrix and by blood and lymph channels. For the membranous tissues of the first group, Adami has proposed the qualifying designation lepidic, and for the pulp tissues of the second group he uses the adjective hylic. The epiblast gives rise to the lepidic epidermis and its derivatives, and to the hylic nervous system tissues. From the hypopblast come the lepidic epithelium of the intestine and of the derivatives of the primitive intestinal tract, and the hylic tissues of the notochord. From the mesoblast are derived the mesothelial and endothelial linings and the specific cells of the organs derived from the middle layer, and the great group of hylic supporting tissues together with the striated musculature.

The fundamental characteristics of lepidic and hylic tissues are, in general, retained by the tumors to which they give rise, and this fact forms the basis of Adami's classification. The matter is not so simple, however, as might be expected from a sharp distinction between lepidic and hylic tissues. It is well known that tumors springing from derivatives of the mesoblast may at times take on the markedly alveolar arrangement characteristic of lepidic tissues, and at other times the diffuse, non-alveolar character of hylic tissues. This tendency is an expression of the ancestry of the cells, which come from a primitive germinal layer originally hylic in character. The mesoblast in the beginning is a pulp tissue; in its further embryologic development it forms tissues which are typically lepidic, namely, the mesothelial linings of the serous cavities, endothelium, and the specific epithelium of the suprarenals and of the urogenital system. It is these tissues which give rise to tumors, at one time lepidic, and at another hylic in nature. The lepidic character of the mesoblastic derivatives is a secondary development in tissues primarily hylic, a fact which manifests itself in the tumors under consideration by the transitional state of the lepidic attributes. In his classification Adami takes this fact into account and overcomes the difficulty raised by this group of tumors by including them in a group to which the heading transitional is applied. Every tumor classification must, of course, make provision for tumors composed of differentiated tissues and tumors of the same origin made up of unripe and undifferentiated tissue. Based upon the considerations which have been outlined above, the classification of Adami is as follows:

I. LEPIDIC, OR "RIND" TUMORS

(A) Lepidomas of the First Order

1. *Of epiblastic origin.*
   Tumors whose characteristic constituents are overgrowths of tissues derived directly from the epiblastic lining membranes, or epiderm.
   - (a) Typical. Papilloma, epidermal adenomata (of sweat, salivary, sebaceous, and mammary glands, etc.).
   - (*b*) Atypical. Squamous epithelioma, carcinoma of glands of epiblastic origin.
2. *Of hypoblastic origin.*
   - (a) Typical. Adenoma and papilloma of digestive and respiratory tracts, thyroid, pancreas, liver, bladder, etc.
   - (b) Atypical. Carcinoma developing in the same organs and regions.

(B) Lepidomas of the Second Order, or Transitional Lepidomas

3. *Of mesothelial origin.*
   Tumors (mesotheliomas) whose characteristic constituents are cells derived in direct descent from the persistent mesothelium of the embryo.
   - (a) Typical. Adenoma of kidney, testicle, ovary, urogenital ducts; adenoma of uterus and prostate; adenomas originating from the serous membranes, "mesothelioma" of pleuræ, peritoneum, etc.
   - (b) Atypical. Cancer of the above-mentioned organs; squamous endothelioma, so-called, of serous surfaces, epithelioma of vagina; adrenal mesotheliomas, hypernephroma.
4. *Endothelial lepidomas.*
   Tumors originating from the endothelium of the blood and lymph vessels; lymphangio-endothelioma, hemangio-endothelioma; perithelioma, cylindroma, psammoma, cholesteatoma.

II. HYLIC, OR "PULP" TUMORS

1. *Of epiblastic origin.*
   Tumors whose characteristic constituents are overgrowths of tissues derived from the embryonic pulp of epiblastic origin.
   - (a) Typical. True neuroma, glioma.
   - (b) Atypical. Gliosarcoma.
2. *Of hypoblastic origin.*
   Tumors derived similarly from embryonic pulp of hypoblastic origin.
   Chordoma.
3. *Of mesenchymal origin.*

(A) MESENCHYMAL HYLOMAS. DERIVED FROM TISSUES ORIGINATING FROM THE PERSISTENT MESOBLASTIC PULP, OR MESENCHYME.

(a) Typical. Fibroma, lipoma, chondroma, osteoma, myxoma, leiomyoma, angioma, myeloma.

(b) Atypical. Sarcoma (derived from mesenchymatous tissues), with its various subdivisions, fibrosarcoma, spindle-celled sarcoma, oat-shaped-celled sarcoma, chondrosarcoma, osteosarcoma, myxosarcoma, lymphosarcoma, chloroma, angiosarcoma; of origin still debated, melanosarcoma.

(B) MESOTHELIAL HYLOMAS. TUMORS WHICH ARE OVERGROWTHS SIMILARLY OF TISSUES DERIVED FROM EMBRYONIC PULP OF DEFINITELY MESOTHELIAL ORIGIN. RHABDOMYOMA

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PART II. GENERAL PATHOLOGY OF TUMORS OF INFANCY AND CHILDHOOD

Structurally many of the tumors of infancy and childhood are peculiar in that it is often impossible to draw a sharp distinction between malformation and tumor. This is due, in part, to the fact that many of them probably originate as malformations or misplacements and attain an organoid character which makes it difficult to group them with the more familiar neoplasms of later life. Such mixed, teratoid or teratomatous tumors occupy a distinct position in tumor pathology and constitute, together with two other groups, the tumors *par excellence* of childhood. The others are the rhabdomyomas and the tumors composed of nervous system elements, both of which, although made up of single cell types as compared with the teratomas, are characterized by origin from cells which normally lose more or less completely the power of proliferation within a variable but probably short period after birth. The teratomas, rhabdomyomas and neurogenous tumors together make up the largest number of neoplasms for which a congenital origin may be accepted. Because of their importance among the juvenile tumors and because, in comparison with the other neoplasms which may occur at any period of life, they are so strikingly the tumors of the early years, they will be considered first, before taking up in order the neoplasms included above in the classification of the autochthonous blastomas.

MIXED TUMORS

The mixed tumors, variously termed also teratoid tumors, teratomas, embryomas, or dermoids, are frequently present at birth, they have been described in fetuses from the third month of pregnancy on, and they are probably all congenital in origin, even if their further development is delayed so that they are not detected until some later period of life. The various designations applied to them are due to their complicated structure, more than one derivative of a single germ layer or derivatives of more than one germ layer being present in the individual tumor. Concerning the origin and nature of these neoplasms there has been much speculation, and many hypotheses have been advanced. Metaplasia, persistence, malformation, misplacement and inclusion have all been emphasized as fundamental factors by such authorities as Askanazy,[1] Borst,[2] Schwalbe,[3] and Wilms.[4] The possibility of the occurrence of these phenomena must be admitted but the mere misplacement of a mass of tissue or its inclusion in other tissues does not explain why, in one case, such a mass differentiates completely and remains dormant indefinitely, to be detected as a chance necropsy finding at some later period of life; in another case differentiates but later gives rise to a malignant tumor; and in still another case fails to form any organoid structures and goes on directly to the formation of a highly invasive and metastasizing neoplasm.

Misplacement.—If misplacement is a factor, as it probably is, the congenital nature of such tumors is established by the fact that such misplacement must occur very early in embryonic life if the misplaced cells are to give rise to the variety of tissues which may occur in the teratomas. Many of the important controversies, which help to make up some of the most important literature relating to this subject, are based upon the varying period in embryonic development in which the misplacement is supposed to have occurred. These controversies are well illustrated by the mixed tumor of the kidney and have been reviewed in the discussion of this tumor in a preceding volume (Chapter CI, Volume IV). If the various tissues which make up a given mixed tumor are all derivatives of a single germ layer, it is necessary to carry the time of misplacement back to a period when the cells of the germ layer are still pluripotent. If the tumor contains derivatives of two layers, then it is necessary to suppose misplacement to have occurred at a still earlier period, when the maldevelopment may have separated off pluripotent cells from two layers, or when the middle layer is still so undifferentiated as itself able to give rise to several kinds of tissue. If the admixture of tissues is still more varied, then it has been supposed that the misplacement has occurred at such an early period that the separated cells are totipotent, that they belong to the blastomere stage before the formation of germ layers has occurred. The experimental production of tumors from misplaced blastomères, claimed to have been accomplished by Bjelogolowy[5] in the frog, and accepted by many as the strongest evidence in favor of the development of teratomas from misplaced blastomeres, has not been confirmed by and is denied by Bierich[6] and by Teutschländer,[7] who claim that the supposed tumors were only inflammatory granulomas.

Parthenogenesis.—The frequency of occurrence of mixed tumors of the ovary and testis introduces parthenogenesis as a factor in the origin of these tumors. If the possibility of parthenogenetic development of the human sex cell is granted, then the pluripotent character of the descendents of such a cell must be admitted and the mixed nature of the tumor is explained. While, at first glance, parthenogenesis might appear to be a factor only in the gonadal mixed tumors, comparative embryologic investigations which have sought to establish the continuity of the germ plasm would, if accepted for the human being, make the phenomenon of parthenogenesis applicable to mixed tumors of childhood situated elsewhere than in the gonads. Cell lineage studies indicate the direct descent of the sex cells, independently of the somatic cells, from the original fertilized ovum; the first localization of these cells in the hind-gut, before the gonads have been formed; and the migration of the sex cells from their primitive extra-gonadal location to the gonads, after differentiation of the latter has begun. The fact that the primitive sex cells must migrate through the mesenteric and retroperitoneal tissues to the ovary and testis would introduce the possibility of failure of complete migration of some of the cells, with their permanent lodgement outside the gonads. From such misplaced sex cells mixed tumors of varying degrees of complexity might arise by parthenogenesis or partial development without fertilization. A most striking example of misplacement of gonadal tissue, which appears to have a bearing upon the question of the migration of the sex cells, is that reported by Nieberle[8] in a hog. Scattered about in both layers of the peritoneum were numerous nodules, more than 100 in each layer, of greyish-brown tissue from a few millimeters to several centimeters in size. Each nodule was surrounded by a fibrous capsule, which was believed to be a tunica albuginea. The parenchyma was composed of well differentiated spermatic tubules, each lined by a single layer of cells, some of which were Sertoli cells, others archispermiocytes. No later stages of spermatogenesis were seen. The tubules were separated from each other by large cells, held to be interstitial cells of Leydig, which are normally numerous in the swine's testis and are especially prominent in the cryptorchid testis of this animal.

Rotter[9] reported the extra-gonadal localization of what he considered to be primitive sex cells in a 7 cm. human embryo of the eleventh to twelfth week of development. Since organogenesis is completed during the tenth week, the occurrence of germ cells outside the gonads at a period later than this was interpreted as evidence that such misplaced cells could not complete their migration and could never reach the sex glands. These cells Rotter conceived to be the possible starting point of tumors. He claimed to be able to identify the cells in the mesorectum, the mesentery, the pancreas, the esophagus, and the retroperitoneal connective tissue. The criticism which can be and has been made against all of the work relating to extra-gonadal sex cells is that the observations may be faulty, since the identification of these cells is based upon morphologic characteristics, by means of which it is claimed to be possible to distinguish between sex cells and soma cells. What are said to be sex cells may not, after all, be sex cells, in view of the uncertainty of the criteria advanced for identification.

Meyer,[10] who granted the continuity of the germ-plasm and the migration of the sex cells, derived the teratomas from misplaced soma cells. These he conceived to be carried along with the sex cells in the migration of the latter, and to be held in a misplaced situation when the latter come to rest outside the gonads. While admitting the migration of the germ cells, he excluded parthogenesis as a factor in the teratomas. Although a number of other pathologists accept the extragonadal formation of the sex cells and their migration, the occurrence of parthenogenetic development of such cells is not granted by most of them. One gains the impression that pathologists refuse to accept parthenogenesis as a factor because its occurrence is foreign to the generally accepted scheme of things among the higher mammals. And yet, if a teratoma ever develops from sex cells, whether the latter are misplaced or not, there must have occurred a succession of cellular divisions with partial differentiation of the resulting cell mass. Such a process is similar to the early development of the fertilized ovum, and it is difficult to see how the application of the term parthenogenesis to this process can be avoided. Parthenogenesis can be certainly excluded as a factor in teratoma formation only if such tumors can arise only from misplaced somatic blastomeres or their misplaced descendents and never from primitive sex cells. The relatively frequent occurrence of ovarian and testicular mixed tumors makes exclusion of sex cells as a beginning of such tumors difficult.

Teratoma.—Variation in the stage of embryonic development at which misplacement occurs results in differing degrees of complexity in the tumors which arise from such misplacements. To express the degree of the resulting variability of structure the terms teratoma, teratoid, and mixed tumor have been used by many writers with restricted meanings. A misplaced primordial germ cell or a blastomere would have the totipotent qualities of the fertilized ovum. It could give rise to derivatives of the three germ layers, and these may go on to practically complete differentiation. There may result a complex anatomical structure with organoid characters, to which the term teratoma is applied. Such teratomas are frequently examples of malformation, rather than of neoplasia, and need show no greater degree of proliferative activity than do the equally differentiated tissues of the host. In this group there are, at one extreme, monstrosities of the reduplication type with a high degree of organoid differentiation, and at the other extreme, structures like the ovarian dermoid, in which there occur well differentiated tissue aggregates, but the latter do not usually imitate very closely the normal organs. Differentiation and organoid structure are the characteristics of teratoma, if the meaning of this latter term is to be restricted or limited.

Teratoid.—If differentiation is less complete, the formation of structures which bear a resemblance to organs does not occur. The component tissue of the mass is more cellular, but the complicated structure of the tumor is evidenced by the formation of elements which can be recognized as derivatives of the three germ layers. To the tumors of this group the designation teratoid has been applied. The teratoma often has a cystic character, the cavity representing a body cavity or body surface. The teratoid is usually more solid, although it may contain multiple small cysts, derived from epithelial lined structures, the spaces representing gland or primitive organ lumens. Schwalb[11] has stressed this difference as it is exemplified by the common dermoid and the less frequent solid teratoid of the ovary.

Mixed Tumor.—The term mixed tumor is often reserved for neoplasms which contain derivatives of only two germinal layers or multiple derivatives of even a single germ layer. In the latter case metaplasia may be conceived to be the fundamental process, or the cells which gave rise to the tumor must have been pluripotent at the time of misplacement. The primitive mesoderm, because of the great variety of structures to which it normally gives rise during embryogenesis, may thus be conceived to give rise to tumors of great complexity. The ectoderm and entoderm, because each may normally form both lepidic and hylic tissues, may also form tumors of considerable complexity, if the origin of the tumor is conceived as dating back to the earliest stages of the ectodermal and entodermal layers.

While, theoretically, such a distinction in the meanings of teratoma, teratoid and mixed tumor might be desirable, as indicating a sharper precision of knowledge, the actual distinction is often difficult to make in any given tumor. Especially if we are dealing with neoplasms rather than with malformation, greater growth energy upon the part of some one constituent may disturb relationships to such a degree as to efface those characteristics upon which the attempted distinction depends. A rapidly growing element may so completely overgrow all the structures originally present that only a single type of undifferentiated tissue is seen, which Ewing[12] has maintained to be the case in the majority of the malignant tumors of the testis. Another complicating factor, to which Borst[2] has called attention, is the failure of certain tissues to develop, because of environmental conditions, although the primitive cell may have had totipotent or pluripotent qualities.

In view of these difficulties it does not appear advisable to attempt to make too sharp a differentiation between teratoma, teratoid and mixed tumor. Following Schwalbe,[3] the terms may be used more or less synonomously, preference being given to mixed tumor. Under mixed tumor we shall not include those blastomas composed of two or more closely related supporting tissues, such as the osteochondrofibroma, fibrolipoma, etc.

Monogerminal or Bigerminal Origin.—Misplacement, metaplasia and parthenogenesis derive the teratomatous tumors from the descendents of the original single fertilized ovum which gives rise to the individual, a monogerminal origin for the tumors of this group strongly supported by Schwalbe. If the tumor arises by inclusion or fusion, a bigerminal origin is postulated, the tumor being derived from a second ovum; the teratoma is the twin of the host. But not all twins arise from separate ova; twinning may be due also to division of the single fertilized ovum into two blastomeres or groups of blastomeres which become separated, each developing into a more or less complete individual. Similarly, the partial division of the early embryo might give rise to monstrosities and teratomas not to be distinguished from those which have arisen from the fusion of twins.

Schwalbe's[3] conception that all the asymmetrical twin monsters and the teratomas are monogerminal in origin and are to be considered stages of an identical process has received its strongest support from the recent experimental work of Stockard.[13] The latter has shown that the completeness of twinning and the degree of separation which results depend upon the stage at which division of the original single embryo occurs and upon the degree of separation of the foci of growth. In unequal twinning with incomplete separation (asymmetrical twin monsters) the growth of the larger portion or autosite inhibits and slows the development of the smaller portion or parasite, until the latter may be represented only by an amorphous, undifferentiated mass of tissue. Although this work does not explain the blastomatous proliferation of teratomas, that fundamental phenomenon of tumor formation and growth which remains unexplained for all tumors, it does give a logical and experimentally well established basis for the derivation of teratomas from the tissues of their carriers and for the homologization of the teratomas with the asymmetrical twin monsters.

Mixed Tumors of Childhood.—The most frequent site of mixed tumor formation in the early years of life is the urogenital system. Within this system, the kidney is more often involved than any other portion.

Kidney.—To the mixed tumor of the kidney the term adenosarcoma has also been applied. Undoubtedly many of the cases reported as sarcoma or carcinoma of the kidney in children have been of this type, in which either the sarcomatous or carcinomatous element has predominated. Although many different kinds of tissue have been described, those most frequently encountered are products of the mesoderm, hence the derivation of the tumor from the primitive renal anlage by Birch-Hirschfeld[14] and from the embryonic kidney by Busse.[15] The fairly frequent occurrence of embryonic striated muscle, and the occasional occurrence of squamous epithelium or of cellular rosettes supposed to come from the nervous system anlage, have led others, notably Wilms[4] and Ribbert,[16] to suppose an origin at a stage of embryogenesis even earlier than the formation of the embryonic kidney, Wilms favoring the undifferent mesoderm and Ribbert the blastomere stage. This tumor has been discussed in the chapter on tumors of the kidney (Volume IV, Chapter CI, p. 1009) to which the reader is referred.

Lower Urogenital Tract.—In the lower genito-urinary tract, tumors composed of a variety of tissues are less frequent than those made up chiefly or wholly of striped muscle. These rhabdomyomas will be considered later. The tumor of the cervix uteri of an adult, to which Pfannenstiel[17] gave the name of "traubiges Sarcom," contained cartilage in addition to striped muscle. Botryoid sarcomas of similar gross appearance constitute the most frequent type of tumor of the vagina in children, but are usually composed of a single variety of tissue. Hauser[18] believed the vaginal sarcoma reported by him in a girl aged six months to be a mixed tumor because of the presence of cells of epithelial type. Hüsler,[19] who described a mixed tumor of the bladder in a male child aged 1½ years, could find only two other recorded mixed tumors of the bladder. Beneke[20] believed the osteochondrosarcoma of the bladder of an old man, described by him, to have arisen from a congenitally misplaced mesodermal anlage.

Testis.—Although a number of rhabdomyomas of the testis in children are reported the true mixed tumors of this organ are usually encountered in the second and third decades of life, rather than during childhood. The average age in the series studied by Schultz and Eisendrath[21] was 29 years. Chevassu, in his tabulation of 61 cases of teratoma of the testis and 59 cases of seminoma (spermatocytoma, Schultz and Eisendrath), found five examples of teratoma in children. Ohkubo,[23] in 1908, reported 13 cases of teratoma of the testis, two being children aged respectively 11 months and 2 years. He collected 107 cases from the previous literature. Thirty-two of these were cystic, and of this group 16 occurred at ages up to eight years and three at the ages from 9 to 17 years. Seventy-five were solid; of these, nine occurred up to the eighth year and two at 9 to 17 years.

Kober[24] tabulated 107 cases of so-called sarcoma of the testis; 10 of 90 cases of this series in which the age was stated occurred in children, but because of the improper application of the term sarcoma to the tumors of the testis, it is impossible to determine how many of these were actually mixed tumors. Koslowski[25] has reported a mixed tumor of the scrotum in an infant aged one year and nine months. This tumor had no connection with the testis; it contained derivatives of the three germ layers, but no striated muscle or bone.

Ovary.—In the adult the ovary is probably the most frequent site of mixed tumor, the lesion usually being of the benign cystic type termed dermoid. In children the ovary ranks next to the kidney, among the organs of the genito-urinary tract, in frequency of involvement by mixed tumor. Both cystic tumors, of the same type as occur in adult women, and solid ones, which are infrequent in women, are encountered. Schwalb,[11] Ingier,[26] Sjövall,[27] who reported three cases of solid mixed tumor in girls, and Franco,[28] who reported one case, have discussed the theoretical relationships of these two types of tumor to each other. Of cystic dermoids in children, the case reported by Shattock[29] presented unusual features in that the ovarian tumor contained a complicated mass in which could be recognized a hydrocephalic brain, 5.5 by 3 cm. in size, which was lined by ependyma. The age of the child which bore this tumor was 2 1/2 years. The age incidence of 49 cystic and solid ovarian mixed tumors, occurring during the first 15 years of life, was found by Merkel[30] to rise as puberty was approached. In 60 cases of ovarian tumor in children 10 years of age or under reported up to 1904 and tabulated by Wiel,[31] 21 were mixed tumors. In 26 additional tumors of the ovary at 10 years or under, Downes[32] found eight mixed tumors. The benign cystic dermoids may remain unrecognized clinically unless their size makes an abdominal tumor evident or unless acute symptoms develop as the result of twisting of the pedicle.

The solid tumors are frequently malignant, the malignant element having been termed sarcoma (Hicks and Targett[33]), neuroblastoma (Neuhauser[34]), or carcinoma (Harris[35]). As already mentioned in the discussion of the relation of gonadal tumors to abnormal development, sexual precocity was present in the cases of Harris, aged 5 years and 10 months, and of Fusino,[36] aged six years. The symptoms of the solid mixed tumor may be those of a progressively developing abdominal tumor, or they may come on suddenly when torsion of the pedicle of the tumor occurs (Winternitz and v. Finlay[37]). Harris, who reported his case in 1917, tabulated 21 cases from the previous literature. The age in this group of 22 cases was as follows: 3 to 4 years, 3; 5 years, 1; 6 to 7 years, 4; 8 years, 2; 9 years, 3; 11 years, 1; 12 years, 2; 13 years, 1; 14 years, 5. The right ovary was involved in six cases, the left in nine, both ovaries in one (Kartuschanskaja),[38] and in six cases the localization was not stated. In eight cases operation was followed by recurrence and metastasis, the latter usually being in the peritoneum and liver.

Polar Mixed Tumors.—Perhaps next in frequency to the mixed tumors of the urogenital system come those arising at the poles of the body, where reduplications and other anomalies are also frequent. The gradation from complex parasitic monster to simple, apparently homologous blastoma is nowhere better illustrated than in this group. At the cranial end occur, as examples of greatest complexity, epignathi which are attached to the maxillary region of the host only by an umbilical cord; at the caudal end, the parasitic pygopagi are usually more broadly attached. At the other extreme of the series are the hairy polyps of the pharynx and the tail-like lipomas of the sacral region. That any single explanation of the origin of such an apparently heterogeneous mass of structures will be acceptable to all is hardly to be expected. The chief controversy has related to the bigerminal or monogerminal origin of the polar parasites and teratomas. Calbert,[39] Stolper[40] and perhaps the majority of pathologists and teratologists have accepted a bigerminal origin for the entire group. Schwalbe[3] believed the epignathi and the cranial teratomas to be monogerminal. Steinemann[41] accepted this view for the sacral teratomas, and Schwalbe finally held the monogerminal origin to apply to all the tumors and asymmetrical monsters of this group. Borst[2] has taken a middle stand, believing that the more complicated parasitic structures are bigerminal, and that the less highly organized teratomas may be monogerminal. Heijl,[42] like Schwalbe, has also emphasized the gradations from monster to mixed tumor, and has laid great stress upon the universal occurrence of embryonic nervous system tissue in these structures, believing that this indicates an attempt at the formation of the cranial end of an embryo, even in the absence of organoid structures.

Cranial Mixed Tumors.—Schwalbe[3] classified the structures of this group, according to their degree of complexity, as follows:

I. A more or less well-developed parasite is attached to the gum or to the neighborhood of the gum of the host by an umbilical cord (epignathus).

II. Projecting from the mouth are fetal parts, recognizable in the gross as such (limbs, sex organs, etc.).

III. Projecting from the mouth is a formless mass, in which organ-like structures are not recognizable; microscopically the structure is that of a teratoma.

IV. A tumor of variable size is attached to the gum or within the oral cavity; the mass is composed of several kinds of tissue without organoid characters.

It is not surprising that malformations should occur in regions like the head and face, where so many fusions, infoldings and regressions must occur to bring about the normal structures. That misplacements should occur in these regions is also to be expected. The degree of misplacement and the stage at which it occurs may explain the various possibilities which result.

The occurrence of congenital fistulas, simple epidermal cysts and mixed tumors of the regions of the nose and the external ear as the result of developmental errors has been discussed by Evans.[43] In Breslau and Rindfleisch's[44] case, one of the earliest cranial teratomas recorded, a polypoid irregular mass projecting from the mouth of a newborn infant, was continuous, by means of a pedicle which penetrated the base of the skull, with an intracranial mass composed of striated muscle, nerves, cartilage, glandular structures, etc. Arnold,[45] in 1868, described a large, congenital, subcutaneous lipomatous mass of the frontal region of a girl aged nine months; this tissue perforated the bone and was continuous with an intracranial mass composed of adipose tissue, cartilage, bone and bone marrow. The same writer,[46] in reporting a hairy polyp of the pharynx in a 13 year old girl, tabulated from the literature previous to 1888, 38 cases which showed all variations from epignathus to the relatively simple mixed tumor described by him. A somewhat similar pharyngeal polyp reported by him[47] in 1870 had led him to conclude at that time that such polyps arose from abnormalities in the formation or closure of the first gill cleft. His second case and the series which he was then able to collect from the literature led him to believe that all were teratomas, although he was unwilling to decide in favor of either a bigerminal or monogerminal origin of the entire group. He granted both possibilities and termed those of monogerminal origin autochthonous. In the group of teratoid pharyngeal polyps belong the hairy polyp reported by Kelly[48] in a female infant aged six weeks, and perhaps also the unusual pedunculated tumor of the tonsil described by Sturm[49] in an 11 year old girl. The latter tumor, which measured 13 by 5 by 4 mm., was composed of striped muscle and mucous glands embedded in vascular fibrous stroma. In this group is also to be

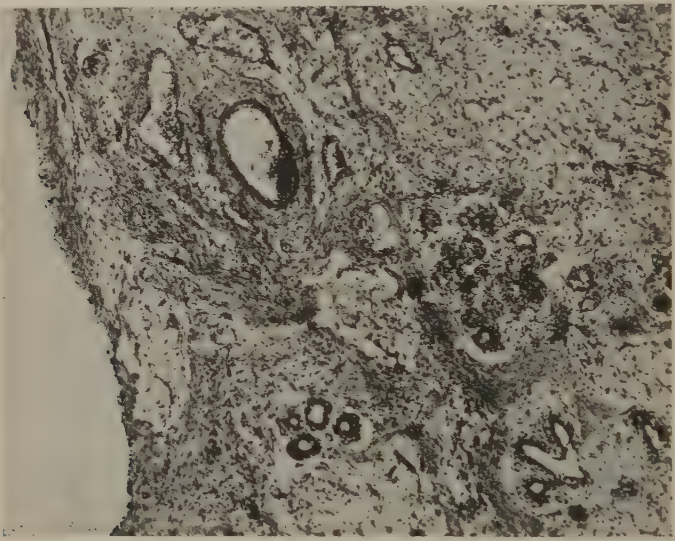

FIG. 274.—Teratoid polyp of pharynx in a newborn infant. Epithelial glands, embryonic mucoid stroma, and neuroglia. ×90.

placed a polypoid pharyngeal tumor of a newborn female infant recently seen by the writer. The pyriform mass, which protruded from the mouth of the child, measured 8 by 4 by 4.5 cm., and was attached by a narrow pedicle to the lateral pharyngeal wall in the region of the hyoid bone. At the point of attachment was an epithelial lined cyst 1.5 cm. in diameter. Microscopically the mass contained cartilage, neuroglia, glands lined by cuboidal and columnar epithelium, bundles of smooth muscle, and embryonic stroma (Fig. 274). Greig[50] has described a pyriform tumor, 1½ in. long, composed of fibrous tissue and smooth muscle, attached at the region of the left frontonasal suture and present at birth. A tumor of the tongue composed of epidermal derivatives, reported by Moschcowitz[51] in a young woman aged 21 years, had been present since early childhood and had ruptured spontaneously when the patient was eight years old. Rupture was followed by a sinus which had persisted in spite of repreated previous operations.

The orbital teratoma reported by Bröer and Weigert[52] in 1876 had a more complicated structure than the above polypoid tumors. It was present at birth, was as large as an apple, and was composed chiefly of adipose tissue, in which were embedded cartilage, bone, epidermal masses and cysts, cylindrical celled mucous cysts, intestinal rudiments, and bronchial elements. Philipp[53] many years later reported a similar orbital, retro-ocular teratoma in a newborn child. A teratoma of an accessory lacrimal gland, reported by Whitham,[54] was composed of adipose tissue, striated muscle, bone and syncytium. The small "dermoids" of the eye and the peri-ocular tissues are composed only of epidermal elements and are apparently derived from misplaced epidermis.

Mixed tumors present within the cranial cavity may be conceived to result from misplacement before or at the time of closure of the anterior part of the medullary groove. They may be situated within the brain substance, in the ventricles, or in the meninges. The teratoma reported by Strassmann and Streeker[55] arose in the choroid plexus of the right lateral ventricle of a boy aged three years, and was composed of a wide variety of derivatives of the ectoderm and mesoderm. Saxer's teratoma of the third ventricle of a seven weeks old child (cited by Eberth[56]) was similarly constituted. The inocuous character which such tumors may have is illustrated by Eberth's[56] chance finding of a mixed tumor composed of mesodermal derivatives, including striated muscle, in the brain of a woman aged 75 years. Cushing's[57] tabulation of 852 brain tumors verified histologically contained four teratomas and eight tumors classified as cholesteatomas and dermoids. Tumors of the latter type, most often situated in the meninges of either brain or cord, are usually composed only of an outer epidermal wall, which encloses a mass of pearly material derived from the epidermal cells. Such tumors should not be included among the mixed tumors, since they appear to arise by separation of cell masses from the already fairly well differentiated unipotent epidermis. In Lauterburg's[58] case, a seven year old boy who died of epidemic encephalitis, the cystic epidermoid tumor lay free in the spinal canal beneath the dura of the cauda. Some tumors of epidermal origin may be somewhat more complicated and may contain derivatives of the epidermis other than squamous epithelium. Frick's case,[59] in an adult, contained sebaceous material and a few hairs. In a bi-lobed cystic tumor described by v. Verebély[60] in a girl aged 14½ years, one apple-sized cyst, which lay free upon the dura of the lumbar cord, was lined in part by ciliated cylindrical epithelium and in part by neuroepithelium; this mass was connected by means of a slender fibrous cord, which penetrated the space between the vertebral arches, with a second subcutaneous cyst of equal size, lined by squamous epithelium with hair follicles and sebaceous and sweat glands.

A tumor of the brain composed of adipose tissue and bone has been reported in an adult by Zuckermann,[61] who cites a lipoma reported by Spieler in a 10 year old boy, and by Bartel in a girl aged 15 years.

Teratomas of the pineal body constitute the most frequent form of tumor of this structure. The relation of such tumors to abnormal development has already been described. One of the earliest reported pineal teratomas with careful microscopic study is that of Weigert,[62] in a boy aged 14 years; the tumor contained cysts lined by cylindrical epithelium, sebaceous and sweat glands, cartilage, fat, medullated nerves, and smooth muscle. Bailey and Jelliffe's[63] tabulation of 60 pineal tumors included 10 teratomas, all of which but one were in children. Five of the pineal teratomas in children were associated with the precocity syndrome.

Globus[64] has reported as a teratoid cyst of the hypophysis, in a girl aged 6 years, a cyst lined by squamous epithelium. Its derivation from the cranio-pharyngeal duct was admitted. Hypophyseal tumors of this type are not infrequent, but they should not be included in the mixed tumor group, since they arise from persistent univalent tissue rather than from persistent or misplaced polyvalent elements.

Mixed Salivary Gland Tumors.—Under the mixed tumors of the cranial pole we may include, for the sake of completeness, the mixed salivary gland tumors of the face, although these usually have no very close similarity with the more complex teratomas, and although there is a tendency among some writers to remove them entirely from the mixed tumor group. Arising usually within or near the parotid gland, they may occur anywhere in the face, lips, buccal cavity, pharynx, or orbit, situations where salivary gland tissue does not normally occur. Concerning their exact nature and the origin of their heterologous elements there has been much controversy, which, up to the present time, has led to no generally accepted opinion. The latter has varied from Volkmann's[65] older view that they are endotheliomatous to Forgue and Roux'[66] more recent conception that they are teratomas. Among later writers, Martini[67] has returned to Volkmann's belief. Others have also considered them derived from single tissue types, but implicate epithelium rather than endothelium, Krompecher[68] believing that they arise from undifferentiated basal epithelial cells, either within the normal salivary gland or in misplaced salivary tissue; Masson and Peyron[69] and Ehrich[70] that they may come from adult glandular epithelium; and Fraser[71] from the epithelium of adult ducts. The objection to the theories which hold a single type of tissue responsible for the mixed salivary tumors is the difficulty of explaining the heterologous mesoblastic tissues which such tumors may contain and which may be cartilage, bone, striated muscle, or mucoid stroma. The occurrence of the last named element might be due to mucoid infiltration of the stroma by the secretion of the cells, a mechanism which Schilling[72] and Böttner,[73] who believe secreting epithelium to be the chief element, hold to be important. It is necessary to fall back upon metaplasia for the explanation of the other mesodermal elements which may be present, if the tumor comes only from endothelium or epithelium. By means of special staining methods Fraser believed that he could actually demonstrate the process of metaplasia of epithelial tumor parenchyma cells to cartilage in some of the parotid and submaxillary tumors studied by him.

Hinsberg,[74] Wood,[75] Vignard and Mouriquand,[76] and others believed that the tumors come from combined epiblastic and mesoblastic misplacements, which arise at the time of the formation of the parotid gland and the branchial arches. Such an origin would account for the presence of bone, cartilage and embryonic stroma, and of the embryonic, gland-like parenchyma, as well as of the squamous epithelium which sometimes occurs. Such a mode of origin would closely relate these tumors to some of the mixed tumors of the neck, which may be structurally much like the salivary tumors. Wilson and Willis[77] concluded that "there is little evidence that these tumors arise from proliferating epithelium, or endothelium," and that "there is considerable evidence to support the theory that these tumors are mesotheliomas of embryonic origin." The last conclusion was based upon the conviction that the parotid anlage appears at about the fourth week of embryonic life, at a time when the mesoblastic tissue into which the gland must grow is quite undifferentiated. But mesoblastic misplacement alone would not account for the presence of the parenchymatous elements of the tumor, unless it is granted that the mesodermic tissue of this region also gives rise to mesothelium. No evidence, either embryologic or from tumors, is advanced to support this statement.

No one theory seems to explain all the tumors of this group, and it is quite possible that not all are of the same origin. In this group, as is the case with the mixed tumors and teratomas elsewhere, the complexity of the tumor may depend upon the potentialities of the anlage which gives rise to the tumor. The presence of only epiblastic and mesoblastic derivatives, in even the most complicated of the salivary tumors, indicates an origin later than that which results in the tryiphyllic teratomas.

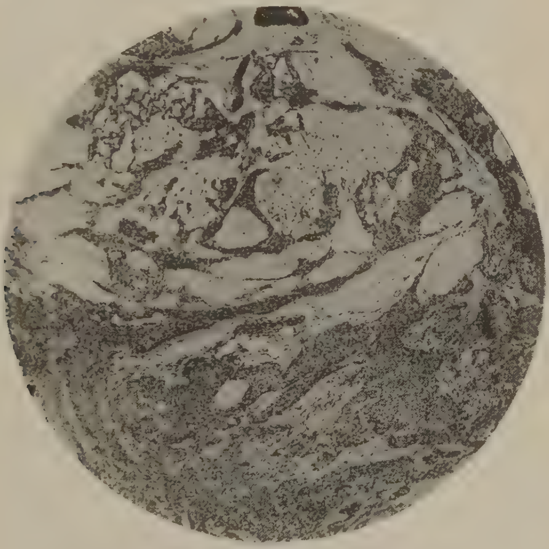

FIG. 275.—Mixed salivary gland tumor of palate. ×60.

The presence of salivary mixed tumors in the eyelids and about the orbit, in the region of the nose, in the lips, or in the buccal mucosa (Fig. 275) is probably due to the complicated processes of fissure formation and fusion which occur in the embryogenesis of the face. Whether the misplacement is the result of the separation of an originally single anlage, or of the primary formation of multiple rudiments in the sense of Albrecht's[78] choristoma or Mathias'[79] progonoma cannot be determined. Woods'[75] series of 59 tumors of this group included 26 of the parotid region, 13 of the submaxillary gland, 4 of the lip, 4 of the pharynx or palate, 2 of the neck, and 1 of the cheek, the latter probably to be included with those of the parotid, since it was in contact with the duct. In 68 cases from the Mayo Clinic studied by New,[80] the locations were as follows: Larynx, 1; sublingual region, 1; cheek, 1; palate, 3; upper lip, 3; pharynx, 4; submaxillary region, 5; parotid, 50. Although these tumors appear to be congenital in origin, they often do not make their appearance until the second or third decade of life. In the combined statistics of Wood and of Wilson and Willis, which include 115 tumors, 4 per cent. arose in the first decade and 10 per cent. in the second decade. Wood's series included one tumor, present since birth in a woman of 27 years, which was associated with aural malformations. Paus'[81] series of 65 tumors, which he considered benign, included only one in the first decade. Paus had also nine tumors which he considered malignant, of which none occurred in the first decade. In a total of 682 tumors tabulated by Paus, 31 or 4.5 per cent. occurred during the first decade. The regional distribution of the 65 tumors of his own series considered benign was as follows: Parotid, 42; lip, 6; submaxillary, 5; orbit, 5; gum, 4; mouth, 2; lower jaw, 1.

The tumors are usually encapsulated. If completely removed they appear to be clinically benign. If removal is incomplete they tend to recur, often becoming histologically and clinically more malignant with each recurrence. Wilson and Willis said that few of the tumors recur after "fairly complete operative removal." This is not in accord with Paus, who, although he considered 65 of his 76 tumors histologically benign, found that recurrence had occurred in 53.2 per cent. of those which had been under observation longer than three years. Of the recurrences he held 24 per cent. to be malignant.

Sacrococcygeal Tumors.—Mixed tumors arising at the caudal pole of the embryo are more numerous than those of the cranial pole. They may be situated within the pelvis, anterior to the sacrum and coccyx and behind the rectum; or posterior to the bony structures and beneath the skin; or, rarely, in the perineal region. Here again the complexity of the tumor appears to depend upon the stage of fetal development at which misplacement occurred. Some of the simpler ones have been held to be due to misplacement of nervous tissue only or to persistence of the neurenteric canal, of the *vestiges médullaires paracoccygiens* of French writers, or of a caudal appendage. The coccygeal gland has also been held to be the site of origin for tumors of this group. Schwalbe's[3] classification of the sacrococcygeal tumors, which may show the same gradations in complexity as those of the cephalic pole, and for which Schwalbe accepted a monogerminal origin, is as follows:

I. A parasitic mass with more or less well developed limbs or organs (pygopagus parasiticus).

II. An external tumor is present, but organs or parts of organs are present only within the mass.

III. Teratomas with derivatives of the three germ layers.

IV. Mixed tumors with derivatives of only two germ layers, usually ectoderm and mesoderm.

The simpler tumors bear somewhat the same relationship to the more complex ones as do the pharyngeal polyps to the cranial teratomas. The gluteal tumor, termed by Virchow[82] hygroma cysticum, present at birth in a female African child, was composed of nerve fibers, glia and striped muscle. Scheuermann[83] reported a congenital sacral tumor, composed of neuroglia in which were a few ganglion cells, in a female child aged three months. The tumor lay between the coccyx and the rectum. Kimpton[84] reported two tumors of the buttock, one a cystic glioma in a boy 14 weeks old and the other a cystic ependymal glioma in a girl aged 14 weeks. Prym's[85] case, in a five year old girl, and the cases credited by him to Depaul and Robin in a newborn child; to Tourneaux and Hermann in a five year old child; to Wieting who had one case in a six weeks old girl and another in a one year old girl; and to Borst, were composed chiefly of embryonic nervous tissue. Prym considered his case a neuroepithelioma or ependymal glioma. These tumors appear to have arisen from misplacements composed chiefly of material derived from the caudal portion of the spinal cord. The tumor which Buzzi[86] described as a sacral angiosarcoma or endothelioma, in a child aged five months, is believed by later authors to have arisen from the coccygeal gland. In a 27 cm. fetus Ribbert[87] described a tumor, situated between rectum and coccyx, composed of a number of cysts lined by cylindrical epithelium, mucus secreting cells, and squamous epithelium. He derived the tumor from the caudal gut and believed that dermoid tumors might arise in this way. Another tumor for which origin from the hind-gut was postulated was the unusual perineal teratoma reported by Albrecht[88] in an individual aged 18 years. The malformation had been present since birth and consisted of an anterior hypospadiac penis, two testes in a divided scrotum, a tumor mass composed of epithelial lined cysts of intestinal origin, and an accessory posterior penis. In spite of the wealth of male genitalia, the individual had been brought up as a female. Schmidt,[88] who reported two coccygeal tumors, one in a fetus of the eighth month and one in a girl aged four years, concluded that the coccygeal gland is probably never a source of origin for coccygeal teratomas. Sklawunos[90] considered the tumor described by him important because he felt that its period of origin could be placed within rather narrow limits, that is, at some time between the end of gastrulation and the formation of the *vestiges coccygiens*, the latter occurring in the fourth fetal month.

In the urogenital system, it has sometimes been difficult to decide whether tumors composed largely of striped muscle should be placed among the homologous rhabdomyomas or among the heterologous teratomas. Marchand[91] raised the same question in connection with an embryonic striped muscle tumor situated over the tuber ischii in a girl aged four years. He placed the tumor among the caudal teratoid tumors. One of the most interesting tumors of this entire group is that reported by Heinzmann.[92] A female child was born with a tumor the size of a hen's egg in the sacral region. The mass was removed when the child was six weeks old; the diagnosis was cystic sacral tumor. Ten years later she returned with a tumor the size of a child's head in the same region. This tumor, upon removal, was found to contain well differentiated derivatives of the three germ layers, including bones believed to represent phalanges. It seems necessary to conclude that the tissue left behind at the first operation retained its totipotent qualities and was able to form derivatives of the three germ layers. A distinction which has been made between teratoma and teratoid by some writers, who attempt to use these terms precisely, is based upon the age of the constituent tissues, the teratoma being composed of tissues as old as those of the host, the teratoid of younger and less completely differentiated tissues. Heinzmann's tumor, from this viewpoint, was a typical teratoma, yet it must have developed from an undifferentiated anlage, not completely removed at the first operation.

Schramm,[93] who reported seven cases of sacral tumor of variable complexity in children, believed that the simpler ones are derived from the neurenteric canal and that the more complex ones are the result of fetal inclusion. Parin[94] was able to collect from the German literature of 1900 to 1909 inclusive fifteen cases of sacrococcygeal teratoma in children; he included only those which were situated anterior to the sacrum.

Pandali, Forsyth and Stewart[95] have reported a sacrococcygeal teratoma which contained carcinomatous tissue and a nodule which was believed to be chordoma; the tumor came from a 12 months old female child. Henning[96] had previously described the occurrence of chordomatous tissue in such a teratoma of a fetus of the seventh month. This unusual element is derived from misplaced notochord tissue; its presence in a teratoma may permit a closer estimation of the fetal stage at which misplacement occurred.

Removal of sacrococcygeal tumors has been successful in a certain proportion of cases. It becomes difficult when the tumor has connections with the spinal canal, or with the terminal portions of the intestinal or urogenital systems, which may also be the seat of malformations. If any of the elements of the tumor have taken on blastomatous properties, removal may be followed by recurrence of malignant tissue.

Teratomas of the Neck.—Mixed tumors of the neck may arise from misplacements associated with the formation of the gill clefts or with persistence of parts of these structures. Most of the neck teratomas appear to have arisen in the thyroid.

Poult[97] observed such a tumor in a male infant shortly after birth. The tumor, removed when the child was 6½ weeks old, contained a few thyroid follicles, but was composed chiefly of heterologous derivatives of the three germ layers. He explained the origin of the tumor by the opening of the second gill cleft into the pharyngeal pouch at the point where the thyroid anlage arises. He collected from the literature five other teratomas of the thyroid in children (one was in an adult but had been present since the fifteenth year of life) and eight teratomas of the neck in children, the tumors not being connected with thyroid. Of the latter group, some were external pedunculated tumors. One ruptured during the delivery of the child, emptying bones and hair, and one, from which bones, teeth and striped muscle were removed, recurred several times after operation.

In two cases reported by Flesch and Winternitz,[98] one in a girl aged eight months and the other in a girl aged two months, the tumor in each case had replaced the thyroid isthmus. The triphyllic tumor of the neck described by Hunziker[99] was so large that it interfered with the delivery of the child and necessitated perforation of the cranium. This author believed that such maldevelopments were due to tissue misplaced by the formation of the gill clefts. Ehlers,[100] who reported a tridermic teratoma removed surgically from the right side of the neck of a male child aged nine weeks, ascribed the mixed tumors of the neck and thyroid to tissue misplaced by the descent of the middle thyroid anlage which forms the isthmus.

Teratomas of the Trunk.—In the teratomas of the trunk there are again all gradations from the asymmetrical parasitic monsters like the thoracopagi, to mixed histioid tumors. The latter, however, are much more apt to be situated internally than is the case with the polar teratomas, and they may be looked upon as developing from blastomeric or pluripotent inclusions arising during gastrulations or before the body walls are completely formed or fused. Incomplete migration of primordial sex cells may, as has already been pointed out, account for some of the tumors arising within the abdominal cavity.

Intrathoracic Mixed Tumors.—Within the chest, teratomas, often termed dermoids, may be situated in the mediastinum, within the lungs, or within the pericardium, being then sometimes attached to the heart or great vessels. The tumor may contain derivatives chiefly of the ectoderm, to which the designation dermoid or epidermoid cyst is restricted by some writers. In about an equal number of instances it has contained also bone, striped muscle, and respiratory and alimentary system derivatives, that is, elements coming from the three germ layers. The tumors of the mediastinum outnumber those of the lung and heart combined, those within the pericardium or attached to the great vessels being exceedingly rare. Joel,[101] who reported an intrapericardial teratoma attached to the pulmonary artery, could find no similar case in the literature to 1890. This tumor caused the sudden death of a boy aged 14 years. Joel believed the tumor to have arisen from a misplaced portion of lung anlage. Bacigalupo[102] reported a second intrapericardial dermoid in 1918 and considered his the only case on record. The mediastinal teratomas may not produce symptoms until adult life; most of the reported tumors have, therefore, been seen in adults. Of a total of thirty-eight mediastinal tumors in children collected by Rosenson,[103] six were teratomas.

Mixed tumors of the lung may be subpleural or they may be embedded within the lung itself. The latter may rupture into a bronchus, a condition which may be followed by expectoration of hair, teeth or other constituents of the tumor. Degenerative changes within the tumor, associated with inflammatory changes about it, may make it difficult to determine whether the tumor was situated primarily in the lung. Hertzler,[104] who collected the reported cases of intrathoracic teratoma to 1916, listed fourteen as teratomas of the lung. Many more were attached to a bronchus or embedded within the lung, but that these arose within the lung appeared doubtful. In 62 cases of teratoma within the chest, analyzed by Hertzler, where age and sex were given, 4 occurred before the tenth year of age, all in females, and 8 between the tenth and twentieth years, 4 being in males and 4 in females. The largest number, 23, were found in the third decade.

The tumors may be malignant, when, of course, they are rapidly invasive and destructive. Malignancy is, however, rare and among the rather large number of tumors recorded was noted only in the cases of Virchow,[105] Jores,[106] and Daugschat.[107]

Intra-abdominal Mixed Tumors.—These may be situated within the mesentery or retro-peritoneally. Lebert's[108] older tabulation of dermoids in general included two of the mesentery, the age not being stated. Niosi,[109] in a thorough discussion of mesenteric cysts, included the dermoids or teratomas as one of the four groups into which he divided these cysts. He was able to collect 13 cases of mesenteric dermoid reported after Lebert's collection; of these one occurred in a child two years old and one in a girl aged 19 years. Merkel[30] includes three mesenteric teratomas at 2, 4 and 12 years of age respectively, and two retroperitoneal teratomas, one in a two year old male and one in a girl aged seven years.

The abdominal teratomas may reach such a high degree of differentiation and organoid development that they have been considered by some to be examples of fetus in fetu, as in the case reported by Rosenbach[110] in a three year old boy. A remarkable example of twin abdominal teratoma is one briefly discussed in the *Lancet*.[111] A slowly increasing swelling of the left side of the abdomen had been present in a male aged 22 years since the second year of life. At operation there were found two fetuses, one 10 in. long with a single upper limb, and a single lower extremity, the other about half the size and less complete. The condition was held to be, not an example of fetus in fetu, but a twin teratoma arising by parthenogenesis from misplaced gonocytes which should have disappeared when they failed to reach the testis.

Sommer,[112] who collected from the literature previous to 1921–22 simple epidermoid cysts of the mesentery, all but one of which were in adults, made a sharp distinction between these and the more complex tumors. He believed that the latter might arise in the ovary, lose their connection with this organ at an early stage, and develop further independently.

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RHABDOMYOMA

Often congenital in origin like the teratomas, genetically similar in certain respects to the teratomas, included by many among the latter, and constituting a group of tumors more characteristic of the earlier than of the later years of life are the rhabdomyomas. Striped muscle is a frequent constituent of the more complicated teratomas and has been described in the somewhat simpler mixed tumors of the kidney. In such tumors the muscle elements are only one result of the process which leads to the formation of a variety of heterologous tissues from totipotent or pluripotent cell substance. There are also, however, tumors composed only of embryonic striated muscle or sarcoblastic tissue. Such tumors may be heterologous, in that they arise in situations which do not normally contain striped muscle. They may be considered homologous when they arise in regions which normally do contain such muscle. In the case of the heterologous rhabdomyomas, the genetic relationship to teratoma is shown by their predominating occurrence in those regions where teratomas are most prone to develop, namely, the urogenital system and the poles of the body.

Metaplasia.—In these tumors the possibility of derivation of the striated from unstriated muscle by metaplasia has been widely discussed. If such a process occurs it would give a simple explanation of the origin of the rhabdomyomas in situations where striated muscle does not normally occur, because unstriated muscle is so wide-spread in its distribution. This very fact speaks against the rôle of metaplasia, since rhabdomyomas should, if this were a process which can readily take place, be more universal in their distribution than is the case.

While the two kinds of muscle may be considered to be closely related because of their common property of contractility and because both are derivatives of the mesoderm, their embryogenetic relationship is not much closer than that of any other two derivatives of the middle germ layer. Differentiation of striated and unstriated muscle occurs early, and thereafter a transformation of one into the other does not appear readily to take place. Carey[1] has described the transformation of the pale smooth muscle of the dog's urinary bladder into red striated muscle as the result of maintaining an increased tensional stimulus within the bladder over a long period of time. Development of rhabdomyoma from a smooth muscle ground substance might be conceived to be possible after a stage of dedifferentiation or anaplasia, if we grant that smooth muscle may return to a completely undifferentiated sarcoblastic condition. Such a process is theoretically and philosophically of great interest in tumor formation, but its actual rôle is difficult to establish. Anaplasia of smooth muscle, with later partial differentiation to striated muscle, would not, however, be metaplasia. The latter process appears inadequate to explain the origin of the heterologous rhabdomyomas.

Misplacement.—Ribbert,[2] earlier in his career, was a staunch upholder of the doctrine of metaplasia, but wider experience with rhabdomyomas in various situations, other than in the pelvis of the kidney, upon which his first conclusions were based, led him[3] to believe that the rhabdomyomas, especially of the urogenital tract, were the result of misplacement, either of undifferentiated mesodermal striated muscle anlage or of mesodermal cellular material so undifferentiated that it could give rise to striated muscle as well as to a variety of other elements. The similarity of this conception to that which derives the teratomas from totipotent or pluripotent cells is apparent. Marchand,[4] as the result of the study of a rhabdomyoma which arose from the anterior surface of the sacrum and invaded the bones of the pelvis, correlated this rhabdomyoma with the caudal teratomas. Berka[5] reached a similar conclusion in regard to the rhabdomyomas of the vagina, as did Himwich,[6] who studied such a tumor originating in the ovary. The theory of embryonic misplacement appears to be the most satisfactory one for the group of the heterologous rhabdomyomas. If the tumor is a pure striped muscle neoplasm, the misplacement may be conceived to involve mesodermal tissue which has already reached the stage of embryonic striated muscle formation; the misplacement would arise at a later stage of embryogenesis than that in which occurs the misplacement of totipotent or pluripotent tissue which can give rise to teratomas or mixed tumors.

Homologous Rhabdomyomas.—When the tumors under discussion arise in situations which normally contain striated muscle, the latter may properly be considered the material which gives origin to the tumor. But even in the tumors of this group, embryonic maldevelopment appears to be a necessary precursor of tumor formation, since the tumors are also usually congenital in origin or arise early in life. If it were possible for normally differentiated striped muscle to give rise to tumors, then rhabdomyomas should occur much more frequently in adult life than is actually the case. For the homologous muscle tumors it may not be necessary to presuppose misplacement, but it does seem necessary to believe that a process of failure or inhibition of differentiation of embryonic tissue is essential.

Histology of Rhabdomyoma.—The rhabdomyomas are usually composed of cellular young tissue which has the structure of embryonic striated muscle. The youngest cells are often unstriated, they may be branched, because of which they have been termed "spider cells," and they may be united with each other to form syncytial mass. As differentiation occurs the peripheral portions of the cells first become fibrillated, the nucleus remaining surrounded by a zone of undifferentiated cytoplasm (Fig. 276). The cells are often vacuolated and may contain large amounts of glycogen. Even in cells which exhibit quite distinct fibrillation, there is rarely the formation of typical muscle fibers, in that the nucleus tends to maintain a central or nearly central position, instead of the peripheral location which is normal. In this respect, as well as in the tendency to branching, the cells of the rhabdomyoma are more like those of cardiac muscle than of voluntary muscle. In this connection it is of interest to note that rhabdomyomas, when apparently homologous, occur much more frequently in the heart than elsewhere. Perhaps the final stage of differentiation which normal cardiac muscle reaches may be looked upon as nearer the embryologic condition than is the case with fully developed voluntary muscle. The rhabdomyomas are frequently malignant. They are then composed of an undifferentiated cellular tissue which can not be distinguished from some of the ordinary forms of sarcoma unless striation and fibrillation can be detected in some of the cells which reach this stage of differentiation. Even in metastases there may occur a degree of differentiation sufficient to permit recognition of the tumor as a rhabdomyoma. The malignant tumors of this group are termed rhabdomyosarcomas or rhabdomyoblastomas.

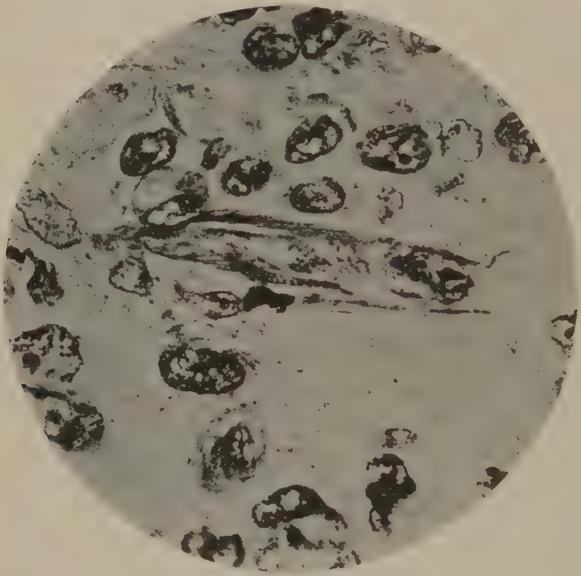

Fig. 276.—Rhabdomyoma of voluntary musculature. An elongated cell with partial cross striation. (Burgess.[34])

Rhabdomyomas of the Urogenital System.—Kidney.—The pure muscle tumors of the kidney may reach a large size. Perhaps the first reported case is that of Eberth[7] (1872), in a 17 months old female child. This tumor had given rise to diaphragmatic metastases whose muscular character was recognizable. Eberth did not consider metaplasia a satisfactory explanation of the origin of this tumor, but believed that it arose from embryonic striated muscle tissue misplaced into the kidney. Cohnheim and Lundsberger, according to Marchand,[8] reported similar renal tumors in 1875 and 1877 respectively. In Marchands' case, a male infant aged 16 months, the tumor, which was inoperable, weighed 2770 gms. This writer also believed that metaplasia was an unsatisfactory explanation for the origin of such tumors and called attention to the frequent occurrence of striped muscle in the teratoid tumors of the urogenital tract. Unless the absence of other heterologous tissues in congenital renal tumors is excluded by careful microscopic examination, such tumors which contain striated muscle are probably to be included among the mixed tumors of the kidney. The first tumor reported by Ribbert,[2] in 1886, was a rhabdomyoma of the renal pelvis in a girl of four years. In the later group of tumors studied by Ribbert,[3] there was included one 8 cm. in diameter, which arose from the pelvis of the kidney of a boy aged eight years.

Bladder.—In the bladder a few rhabdomyomas have also been reported. Mönckeberg,[9] who studied such a tumor of the bladder of an adult, refers to one of Vincenti in a boy aged 13 years, one of Cattani in a 12 year old boy, and one of Hüsler in a boy aged seven years.

Vagina.—The first recorded muscle tumor of the vagina is that of Kaschewarowa-Rudnewa[10] (1872), in a girl of 15 years. Removal was followed by recurrence and death. The tumor described by Berka[5] arose from the cervix of the uterus in a girl aged 18 years; hysterectomy was followed by early recurrence and by death within three months. Berka ascribed the origin of his tumor to a misplaced mesodermal rest. Such misplacements be believed to be capable of forming various mesodermal derivatives, and therefore concluded that all the rhabdomyomas of the vagina and uterus should be included among the mixed tumors. McFarland's[11] tabulation of 102 cases of sarcoma of the vagina included 34 example of the botryoid type, all in children under five years of age; in this group there were three myosarcomas and one myofibrosarcoma, but whether the muscle was striated was not stated. Of McFarland's remaining 68 vaginal sarcomas not of the botryoid type, 18 occurred at 17 years or under; this group included two rhabdomyomas and one listed as myosarcoma.

Ovary.—Himwich[6] has described a rhabdomyoma of the ovary of a girl aged 1½ years. The tumor was encapsulated and sprang from the left ovary. Removal was followed by death from abdominal metastasis three months after operation. Vignard[12] had reported a similar solid tumor of the ovary in a 17 year old girl in 1889, and Virchow[13] described a metastasizing cystic rhabdomyoma of the ovary in 1850. These appear to be the only pure muscle tumors of the ovary on record.

Prostate.—A tumor which measured 6.6 by 4.0 cm. and which arose from the prostate of a boy aged nine months has recently been recorded by Sysak.[14] The neoplasm was composed of a spindle-celled sarcomatous ground substance, in which were large polymorphic cells, believed to be embryonic striated muscle cells, although actual striations could not be detected. The author tabulates 22 cases of sarcoma of the prostate in children, the oldest being 10 years of age; three of these tumors were rhabdomyosarcomas.

Testis.—In all the above tumors the striated muscle was heterotopic. In the case of the rhabdomyomas of the testis, a decision as to the heterologous or homologous character of the tumor is more difficult to arrive at, and controversy as to the origin of the testicular rhabdomyomas has existed ever since Rokitansky,[15] in 1849, reported the first case in a youth aged 18 years. Rokitansky believed that the tumor originated from remnants of the striated muscle of the gubernaculum. The tumor reported by Neumann[16] occurred in a boy aged 3½ years and was situated at the lower pole of the testis, in the region of insertion of the gubernaculum. Because of its situation and because it was quite distinct from both the testis and epididymis, Neumann derived the tumor from misplaced gubernaculum muscle and concluded that the testicular rhabdomyomas should not be included among the teratomas. Ribbert's[3] series of rhabdomyomas included two of the testis, one in a boy aged 13 years, the other in a boy aged 14 years. In each case the tumor had replaced most of the testis; in the first one the tail of the epididymis was still recognizable, but

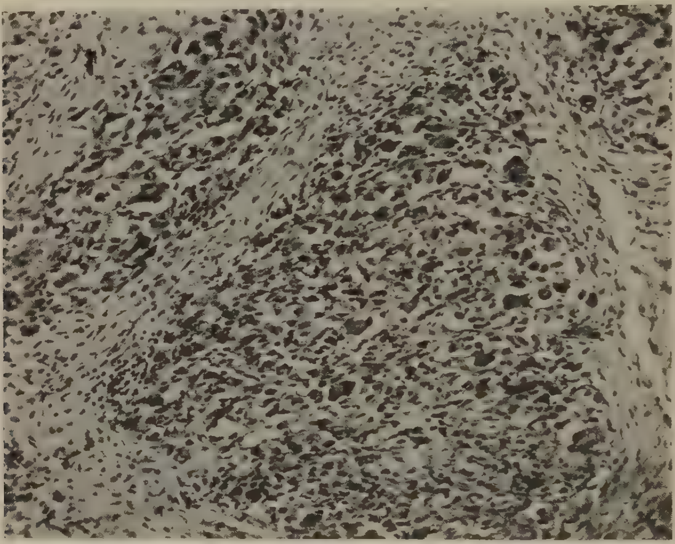

FIG. 277.—Rhabdomyoblastoma of ectopic testis of a child aged 2 months. ×150.

in the second nothing of either testis or epididymis could be found. That Ribbert derived all the urogenital rhabdomyomas from mesoblastic misplacements has already been stated. Becker,[17] who reported a case of bilateral rhabdomyoma of the testis in an adult, considered the possibility of origin from the internal cremaster muscle by metaplasia or directly from the striped muscle of the gubernaculum, and excluded misplacement as a source of the testicular rhabdomyomas. Arnold[18] reported a rhabdomyoma of the testis in a boy aged four years; only a few tubules of the epididymis could be recognized, all the rest of the tissue of the epididymis and all of the testis having been replaced by tumor tissue. The giant cell sarcoma of the tunics of the testis, reported by Fischer and Wolters,[19] in a boy aged 16 years, may have been a rhabdomyoblastoma. During the preparation of the manuscript the writer had the opportunity of studying a rhabdomyoblastoma of the undescended testis of a child aged two months. The spherical tumor measured 12 cm. in diameter. None of the original structural elements of the testis or epididymis could be found. Five months after removal of the tumor the local recurrence measured 7 by 5.5 by 4.5 cm., and the peritoneum was found studded with metastases at a second operation at this time. The tissue was composed of elongated spindle cells and of giant cells, in some of which faint striation could be demonstrated (Fig. 277).

Polar Rhabdomyomas.—The polar rhabdomyomas may be considered closely related to the cranial and sacral teratomas. Zenker[20] reported such a tumor of the orbit in boy aged seven years, the neoplasm having first been noticed when the child was five years old. It was composed of embryonic striated muscle, and recurred twice, finally causing death. Zenker could find only one other reported case of orbital rhabdomyoma, that of Bayer. Erdmann[21] studied a tumor, present since birth, situated on the bridge of the nose of a child aged seven months. It was made up of both well differentiated and embryonic striped muscle. Nicory[22] has recently reported a rhabdomyoma of the uvula of a girl of five years. When first noticed by the mother it was about 4 mm. in diameter; a month later it had increased to 2 cm. and the uvula was transformed into a thin pedicle. Removal was followed by recurrence, the entire soft palate being involved in an inoperable tumor mass. The original neoplasm was composed of sarcoblasts in a cellular, sarcomatous ground substance; distinct cross striation was present in the embryonic muscle cells. Nicory believed the tumor to be due to misplacement of embryonic muscle cells, although he considered also the possibility of teratoma.

Marchand's tumor,[4] which apparently arose from the anterior surface of the sacrum and which had invaded the tuber ischii, was held by him to be closely related to the sacrococcygeal teratomas, although he could find no heterologous elements other than striated embryonic muscle rich in glycogen. In Ribbert's[3] series there was one rhabdomyoma of the temporal region in a girl aged 1½ year, and one of the jaw in a boy. Whether these tumors are to be placed among those which arise at the cranial pole as the result of misplacement, or among the homologous tumors arising from normally situated striated muscle can not be determined. The former appears more probable.

Rhabdomyoma of the Heart.—Of the homologous rhabdomyomas, those of the heart are by far the most frequent and constitute the most interesting group. They are very often multiple and usually have the appearance of islands of cardiac muscle whose normal development and differentiation have been inhibited, rather than of blastomatous new formations. Such areas are composed of syncytial groups of vacuolated "spider cells," whose peripheral cytoplasm may show varying degrees of striation. In the case reported by Knox and Schorer,[23] in a colored child seven months old, the cavity of the left ventricle was almost filled by a pedunculated tumor 2 cm. long; other nodules from 3 mm. to 1 cm. in diameter were present within the muscle (Fig. 278). Some writers have believed that the tissue arises from the Purkinje cells of the conduction system and not from the general musculature of the heart. In the specimen recorded by Virchow,[24] from a still-born infant, the embryonic muscle formed the walls of wide, cavernous, anastamosing blood spaces. Abricosoff,[25] who reported a case in a girl aged three years and four months, called attention to the similarity of the rhabdomyomatous tissue to embryonic cardiac muscle at that stage of development when syncytial union of the cells is still evident but striation has begun; he also emphasized the fact that the tissue often appears degenerated. He believed that the tumors

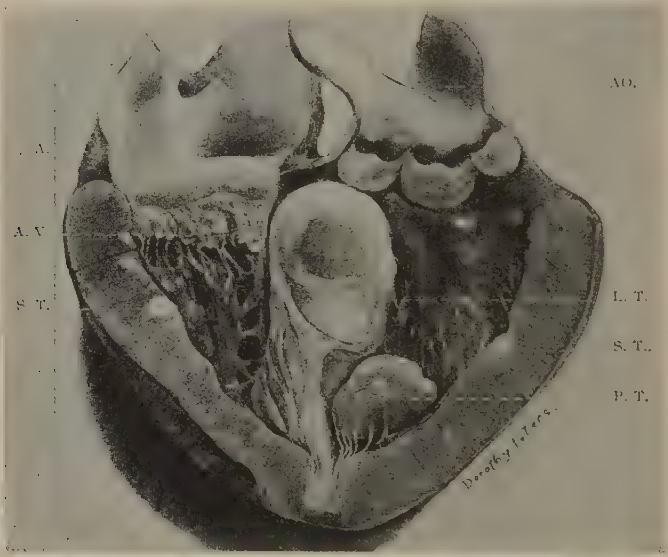

FIG. 278.—Multiple rhabdomyoma of heart. A, auricle. AV, auriculoventricular valve. AO, aorta. LT, large tumor of left ventricle. PT, pedunculated tumor of left ventricle. ST, small tumors embedded in ventricular myocardium. (Knox and Schorer.[23])

were derived from embryonic cardiac tissue which had not differentiated into Purkinje cells and chamber musculature. Degenerative, rather than active proliferative changes, have been frequently noted.

Although some of the reported rhabdomyomas of the heart became transformed into nodular, growing, true tumor masses, most have been of such a character as to lead one to place them among the maldevelopments rather than among the neoplasms. This is further borne out by the great frequency with which rhabdomyoma of the heart is associated with other maldevelopments, especially malformations of the kidney and, in a surprisingly large proportion of cases, with tuberous sclerosis of the brain, which is apparently a condition of multiple foci of congenital excess formation of glia. In Wolbach's[26] case there were multiple nests of neuroglia tissue in the meninges of the spinal cord. In Bundschuh's[27] case, a girl aged two years, there was also a meningeal gliomatous mass attached to the dura in the region of the torcular. In addition, there were multiple areas of tuberous sclerosis of the cerebrum, and multiple small nodules in the cortex of each kidney composed of convoluted tubular epithelium which had not yet formed tubules, and of adipose tissue, smooth muscle, tortuous blood vessels and embryonic glomeruli. Jonas,[28] who reported a case in a boy aged six months, paid greater attention to the brain involvement than to that of the heart, as did Bundschuh. In Jonas' case the surface of the cerebrum was free of the characteristic tuberous nodules, but the entire white matter of the cerebrum from ventricular ependyma to cortex was studded with multiple small areas composed of large cells, which were considered to be embryonic ameboid glia cells.

The cardiac condition rarely causes symptoms. If marked enough, it may apparently cause death immediately after birth or within the first few days thereafter. If the child lives beyond this period, the heart condition does not usually appear to be a factor in death. The associated cerebral lesion leads to failure of mental development and to epileptiform convulsive seizures. Tuberous sclerosis is often associated with adenoma sebaceum of the face. The correct antemortem diagnosis of tuberous sclerosis has been made a number of times. When the clinical condition is such as to suggest this diagnosis, especial study should be made of the heart, because of the frequent association of rhabdomyoma. Such study may lead to the discovery of functional changes which have thus far gone unrecognized. Males are much more frequently affected by tuberous sclerosis than are females, 70 per cent. of 58 cases having been males and 30 per cent. females, according to Bundschuh. The latter was able to tabulate 18 cases of rhabdomyoma of the heart up to 1912.

Amersbach and Handorn[11] reported a solitary rhabdomyoma of the left ventricular wall in an infant aged seven days. The tumor involved the region of the left branch of the atrioventricular conduction bundle, but microscopically was quite distinct from the conduction tissue. The authors, therefore, concluded that cardiac rhabdomyoma does not arise from the Purkinje cells but from portions of the general cardiac musculature, which by displacement have lost their normal relationships to the rest of the muscle. In 1921 they were able to tabulate 22 cases of rhabdomyoma of the heart exclusive of their own. The age in this series of cases was as follows: Newborn, 3; 6, 7 and 14 days, 1 each; 2 and 6 months, 1 each; 7 months, 3; 7½, 10 and 12 months, 1 each; 1½, 1¾ and 2 years, 1 each; 3 years, 3; 3⅓ and 6 years, 1 each. In one case the age was not stated. In 15 cases the tumor was multiple, in five it was single, and in three this point was not mentioned. Tuberous sclerosis was present in ten of the 15 cases with multiple tumors, and in the three in which no statement was made in regard to the single or multiple character of the tumor. In three cases with multiple rhabdomyomas and tuberous sclerosis, there were congenital renal tumors. Steinbiss,[11] in 1923, called attention to three cases which Amersbach and Handorn had overlooked, bringing the total number of cases reported since 1862 to twenty-six. The last named author believed that rhabdomyoma of the heart may not be so infrequent as is supposed. In a 10 year period as prosector in an asylum for epileptics, Steinbiss encountered six cases of rhabdomyoma of the heart; this number included two cases previously reported but omitted by Amersbach and Handorn from their tabulation. During this same period he had seen at necropsy 21 cases of tuberous sclerosis, in which group the six cases of rhabdomyoma occurred. Steinbiss' cases bring the total number of cases of rhabdomyoma of the heart to thirty, in twenty-two of which the cardiac condition was associated with tuberous sclerosis. In some of the 30 cases the brain was not examined, and in the soft brain of the new-born the condition of tuberous sclerosis may be overlooked. He therefore concluded that the association of rhabdomyoma with tuberous sclerosis must be an almost constant one and that rhabdomyoma without tuberous sclerosis must be extremely rare. The six cases of Steinbiss differ from the previously reported ones in the greater age which the patients had attained in his series; the age and sex were as follows: 5 years, male; 8 years, male; 10 years, male; 16 years, female; 21 years, female; 35 years, male. Again the greater preponderance of males over females is apparent.

The character of the tissue in the heart lesions and the frequent association with tuberous sclerosis and congenital renal tumors place rhabdomyoma of the heart among the maldevelopments, and make it part of a condition of maldevelopment which involves the body rather widely. The cardiac condition is one of failure of development and of incomplete differentiation of the heart muscle; a process primarily inhibitory in character becomes associated later with degenerative changes, if the individual lives long enough; only rarely is there active growth of the embryonic tissue. The cerebral condition is similar in character; normal differentiation is absent in the involved areas, but there may be slight overgrowth of undifferentiated glial tissue. This process of failure of development may be associated with misplacement of embryonic glial tissue, as in the cases of Wolbach[26] and of Bundschuh.[27] When the kidneys are involved, the condition is again one of failure of development of localized, usually multiple, areas of tissue. Why three tissues so widely different as cardiac muscle, brain and kidney should be the seat of the same kind of developmental anomaly is an interesting but unsolved question. The one thing which these tissues have in common is their highly specialized character, a fact which may make them more susceptible to factors which inhibit or interfere with normal development than is the case with more simply organized tissues.

Rhabdomyomas of Voluntary Musculature.—Benenati,[31] who reported a rhabdomyoma of an undescended testis in a man aged 49 years, collected 65 cases of rhabdomyoma reported previous to 1903. While the number of cardiac cases

cases has been increased since that time and while a few additional cases in other organs have been reported, this tabulation is important as showing the relative organ or regional distribution of this type of tumor. The 65 cases may be classified as follows:

Urogenital System, 39: Kidney, 13; testis, 9; uterus, 6; renal pelvis, 3; vagina, 3; ovary, 2; ovary or uterus (origin undetermined), 1.

Head and Neck, 9: Orbit, 2; temporal region, nose, tongue, parotid, mandible, mediastinum, esophagus, 1 each.

Caudal Region, 4: Lumbar region, hip, ischium, anus, 1 each.

Heart: 8.

Others, 5: Pectoralis major, breast, shoulder, elbow, thigh, 1 each.

It is apparent from the above that rhabdomyomas arising in voluntary muscle must be quite rare. Listed by Benenati, and by those who have followed him, as a rhabdomyoma of the tongue, and included in the above grouping under "Head and Neck," is the case described by Weber[32] in 1854. Enlargement of the tongue began when the patient, a boy, was 14 years old; at 21 years the organ protruded beyond the teeth and was the size of the palm of the hand. The process was diffuse and Weber himself considered the enlargement, which was due to well differentiated muscle fibers, to be the result of glossitis, and the new formation of young muscle, which followed amputation, to be a regenerative process. This case should not be included among the rhabdomyomas of voluntary muscle. Fujinami,[33] who reported a rhabdomyoma of the muscles of the leg in 1900, believed his to be the first undoubted case of true rhabdomyoma of voluntary muscle. Burgess[34] has more recently described a case of metastasizing rhabdomyosarcoma in a young woman aged 19 years, with widespread involvement of the body. The largest tumor was in the thigh muscles, and was believed to have been the primary focus. The tumors were composed of young, undifferentiated, sarcomatous tissue, which contained many multinucleated cells of the myoblast type, in a few of which striation was evident (Fig. 276). Rhabdomyoma, other than that due to heterologous misplacement of embryonic myoblast or to maldevelopment of the heart, appears to be one of the rarest types of neoplasm.

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TUMORS OF NEUROGENOUS ORIGIN

Tumors derived from elements of the nervous system constitute not only one of the most interesting groups of neoplasms in general, because of certain problems relating to their genesis, but also a group of tumors of childhood so important, because of their frequency early in life, as to warrant separate consideration at this point. Tumors composed of or derived from the glia of the brain have long been recognized. They occur frequently in early life as well as later. While their glial origin has been generally accepted, there is a certain amount of evidence that some, at least, do not come from previously normal glia but from misplaced or dormant, undifferentiated glia, and hence are properly to be looked upon as congenital tumors. Whereas the glioma has long been recognized as a tumor composed of one type of nervous system tissue, the recognition of the neurogenous character of certain tumors connected with the peripheral nervous system is comparatively recent, and the development of our knowledge of some of the tumor types of this group is one of the most fascinating chapters of modern histopathology.

The discovery, as long ago as 1870, by Loretz,[1] of a tumor containing well differentiated ganglion cells established the occurrence of neoplasms to which the term ganglioneuroma was applied. Most of these were derived from the sympathetic nervous system. Further study of tumors of the sympathetic system and more exact knowledge of the embryogenesis of this system and of the relation of the adrenal medulla to the sympathetic system, led at a much later period to the recognition of tumors composed of undifferentiated sympathetic formative cells, for which the name neuroblastoma has been most generally accepted. Intermediate between the ripe, differentiated ganglioneuroma at one end of the series and the unripe, undifferentiated neuroblastoma at the other end, are tumors composed in varying degree of both types of tissue and of transitions between the two types, so that we today have a fairly complete series which establishes the relation of neuroblastoma to ganglioneuroma, of both to the intermediate forms, and of all to the tissues of the nervous system. Proof that the chromaffin tissue of the adrenal medulla and of the so-called paraganglia is derived from the sympathetic system added to the increasingly important group of tumors of neurogenous origin the chromaffinomas or paragangliomas. When, furthermore, the origin of certain tumors of the peripheral nerves from essential neurogenous elements rather than from the connective tissue framework of the nerves was placed within the realm of probability, the group of neurogenous tumors was further enlarged by the neurinomas. The neuroblastoma is *par excellence* and almost exclusively a tumor of early infancy and as such is the most important member of the group. But examples of all the other types have been encountered frequently enough in the early years of life to give to all a considerable amount of importance.

Ganglioneuroma.—The typical ganglioneuroma is a firm, encapsulated, pale, more or less nodular mass, whose similarity in texture and color to the common fibromyoma has frequently been noted. The reported examples have varied in size from small masses to tumors measuring 40 by 20 cm. and weighing 6 kg. (Peters[2]), or others which filled the pelvis of a child and extended to the diaphragm. The tumors are composed of nerve fibers arranged in bundles of variable size, which have a tortuous and interlacing course (Fig. 279). Most of the fibers are non-medullated. Moderate numbers of medullated fibers may be present. Both kinds of fibers usually have distinct Schwann sheaths, whose nuclei are often more closely placed than in normal nerves. The most striking elements are the ganglion cells (Fig. 280). These are well differentiated, unipolar, bipolar or multipolar. They may occur singly or in clusters of various sizes scattered about in the denser tissue. Many of the ganglion cells are surrounded by typical periganglionic cellular capsules; others may be naked. Multinucleated forms may occur, Nissl substance may be present, pigmentation is not unusual, and degenerative changes, which may lead to complete calcification of individual cells, are frequent. Naked axis cylinders, often beaded and irregularly swollen, are numerous (Fig. 281). The disproportion between the number of axis cylinders and nerve fibers in relation to the ganglion cells has given rise to discussion. Degeneration and disappearance of ganglion cells with persistence of axis cylinders is believed by most observers to explain this disproportion. Development of nerve fibers from sheath cells, accepted for peripheral nerves, has been held by Friedrich[3] and Schmincke[4] to occur in ganglioneuroma; Wegelin,[5] in a discussion of this question, did not believe that satisfactory evidence of the occurrence of the process had been offered in any ganglioneuroma. Ganglion cells and nerve fibers are supported by a dense connective tissue framework, which carries few blood-vessels. In its typical well differentiated form the tumor is clinically and histologically benign, and may be a chance necropsy finding in a person of

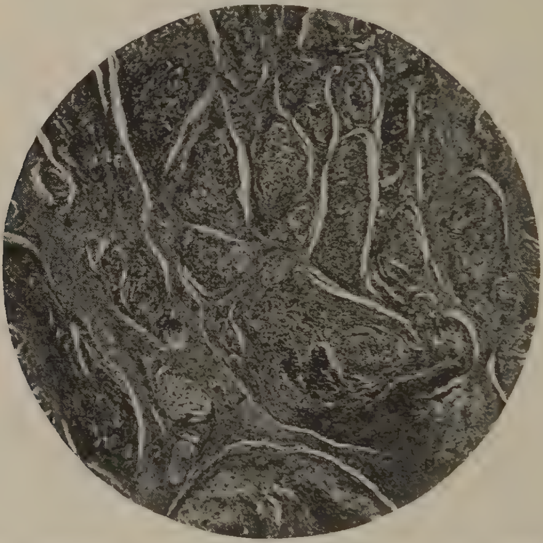

FIG. 279.—Ganglioneuroma of pelvis. Nerve bundles cut in various directions. Child aged 3 months. (Courtesy of Dr. Benj. Roman.[28])

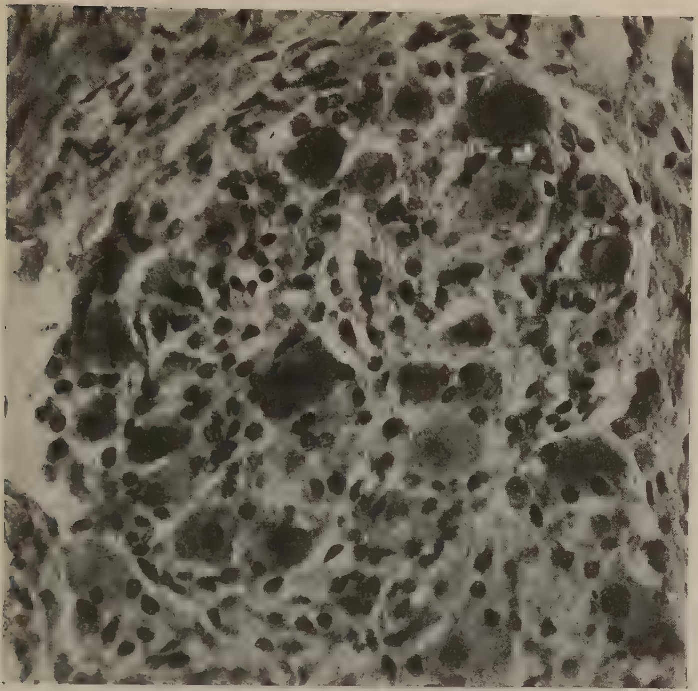

Fig. 280.—Ganglioneuroma of pelvis. Group of ganglion cells. (Courtesy of Dr. Benj. Roman.)

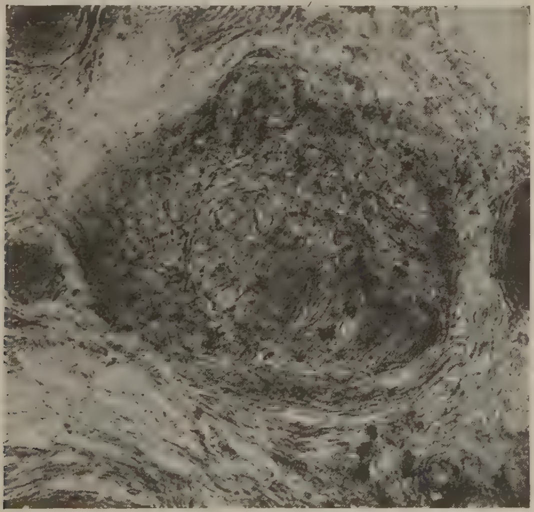

Fig. 281.—Ganglioneuroma of pelvis. Nerve fibrils stained by the Bielschowsky method. (Courtesy of Dr. Benj. Roman.)

advanced age, as in Friedrich's[3] patient, who was a woman 73 years of age. In other cases, and particularly in children, the tumor may cause marked abdominal enlargement or pressure symptoms because of its size.

Location of Ganglioneuroma.—*Brain.*—While this tumor is predominatingly one of the sympathetic system and its closely related adrenal medulla, a few cases have been encountered in the brain and cranial nerves. Schmincke[4] apparently reported the first ganglioneuroma of the brain in 1910. This occurred in a boy aged 17 years, who had had epileptiform seizures since eight years of age; death occurred in such an attack. The tumor, which was firm, walnut sized, and ovoid in shape, was embedded in the right temporal lobe. It was composed of glia and glia cells, ganglion cells, and non-medullated nerve fibers. Pick and Bielschowsky[6] described a similar tumor of the medulla in a woman aged 24 years; they disagreed with Schmincke's belief that the nerve fibers could arise peripherally from sheath cells. In Robertson's[7] case, a girl aged 16 years, symptoms of brain tumor had been present since the age of five years. The tumor, which arose from the floor of the third ventricle and had completely replaced the optic chiasm, was composed of well differentiated tissue, including glia. These three ganglioneuromas of the brain differ from the rest in the presence of glia, and might, therefore, be termed ganglioglioneuroma, as proposed by Robertson for his tumor. Another tumor of this type, although situated in the neck, is the unusual one reported by de Josselin de Jong,[8] in a boy aged one month. The tumor, which was present at birth, increased slowly in size until it extended from the left cheek to the clavicle. It was removed, with no evidence of return up to 14 months after removal. The tumor was composed of a glial ground substance in which were embedded groups of pyramidal ganglion cells like those of the cerebral cortex. There were many nonmedullated nerve fibers. Cystic spaces were present; these were lined by cuboidal epithelium, like typical ependyma. The tumor was believed to have arisen through misplacement of cerebral tissue with complete separation at an early stage of embryonic development. A similar cerebral misplacement ganglioneuroma is that illustrated by Figs. 282 and 283, present at birth in a female child born recently in the maternity service of the Michael Reese Hospital. The hemispherical mass which with the covering scalp measured 2.5 cm. in diameter by 2 cm. in height, was present in the

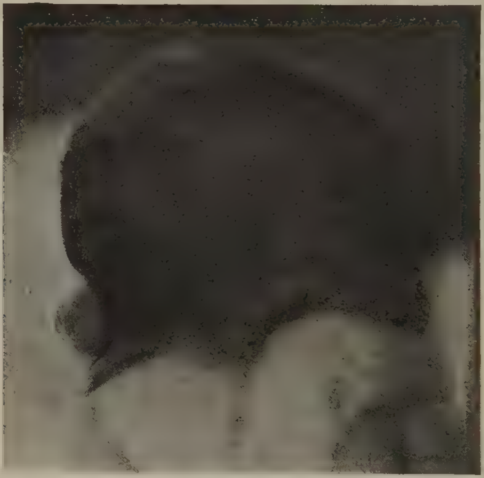

FIG. 282.—Ganglioneuroma of scalp. Newborn infant, maternity service of Michael Reese Hospital.

occipital region. The tumor was removed on the second day of life. The bones of the skull were complete, and there was no connection between the tumor and the brain or its meninges. Within the covering cutaneous tissue was a mass 0.7 cm. in diameter, composed of nerve fibrils and well differentiated neuroglia, in which were embedded a few calcified ganglion cells. The surface of the neurogenous tissue was covered by a thin vascular membrane, which evidently represents the pia. Structures like this and that of de Josselin de Jong illustrate again the narrow dividing line between developmental anomaly and blastoma. In each case misplaced cerebral tissue grew independently of the cerebral tissue from which it arose and differentiated largely along normal lines.

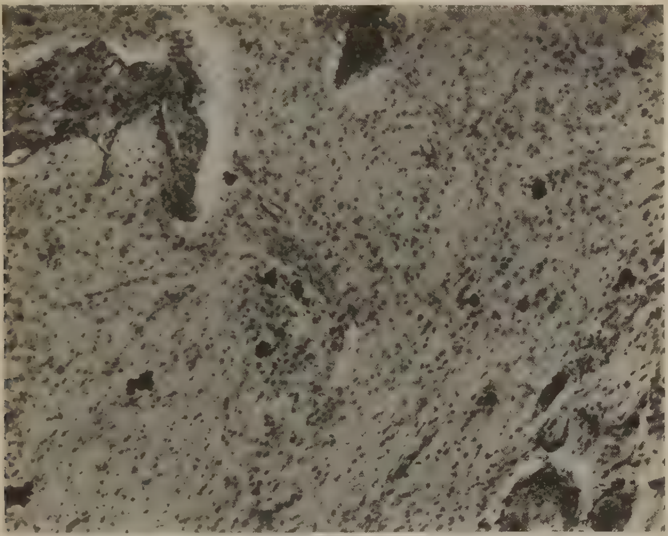

FIG. 283.—Ganglioneuroma of scalp. Well differentiated neuroglia with calcified ganglion cells. ×140.

Cranial Nerves.—Most of the cranial nerve ganglioneuromas have occurred in adults. De Josselin de Jong[8] saw such a tumor of the infra-orbital nerve, removed from the region of the naso-orbital angle, in a child aged 20 months; this contained glia as well as ganglion cells and nerve fibers. Benda[9] reported a ganglioneuroma of the right vagus nerve in a child. Krauss[10] has reported, as an unusual tumor, a ganglioneuroma of the eyelid, which he belived to come from peripheral sympathetic tissue. The tumor was composed largely of non-medullated nerve fibers, but contained also a few small ganglion cells. That such tumors are not more frequently seen in the cranial nerves is surprising, in view of the frequency with which Thomsen[11] was able to find groups of degenerated ganglion cells in the cranial nerves, especially the optic, facial, oculomotor and abducens; he believed these cells had been misplaced during embryonic development.

Cervical Sympathetic.—Ganglioneuromas of the cervical sympathetic have been reported by de Quervain[12] in a 13 year old girl, by Glinski[13] in a 10 year old girl, by Freund[14] in a boy aged six years, by Geymüller[15] in a five year old boy, and by Stout[16] in a girl aged 2½ years. In Freund's case and that of Stout, the tumor was on the right side, in the others on the left side. All of these tumors were successfully removed by operation, which was followed in each case by evidence of interference with sympathetic function, such as ptosis or change in the pupil. The largest tumors were those of Glinski and Freund, which measured 9 by 6.5 by 3.5 cm. and 9 by 6 by 4 cm. respectively. Freund's tumor contained a few small areas of undifferentiated, lymphocyte-like cells, which with the intervening fine fibrils she held to be glia.

Thoracic Sympathetic.—The tumors arising from the thoracic sympathetic have been situated retropleurally in the posterior mediastinum. The three older cases in the literature were in adults. In Tschistowitsch's[17] patient, a girl aged 12 years who died of generalized tuberculosis, the tumor was a chance necropsy finding. It was located on the right side, and extended from the fourth to the sixth thoracic vertebræ. In 1923 Rosenson[18] reported such a tumor in a girl aged eight years. The child had complained of persistent cough, dyspnea, weakness and loss of weight, which symptoms had been present for one year. There was flatness over the right chest. The tumor, which was successfully removed surgically, was the size of a tennis ball; it was made up of well differentiated ganglion cells and nerve fibers and was histologically benign. Stout[16] has reported a case in a boy aged 2½ years, who had been troubled with gastric disturbances for seven months and with weakness of the lower limbs for four months. The tumor, which was on the left side (Fig. 284), caused pressure changes in the spinal cord by ingrowth through an intervertebral foramen. Death followed the attempt at removal. Brunner,[19] in 1924, reported a ganglioneuroma in a girl aged 19 years. The roentgenogram showed the presence of a mediastinal tumor extending from the vertebral column almost to the left lateral margin of the thorax. The tumor, which was removed surgically, measured 17 by 12 by 8 cm. and was encapsulated, pale and firm. It contained bundles of nerve fibers, mostly non-medullated, but some medullated, and numerous multipolar ganglion cells, some of which were vacuolated and degenerated. Operation in this case was followed by infection, empyema, and complete sequestration of the left lung, but by ultimate recovery.

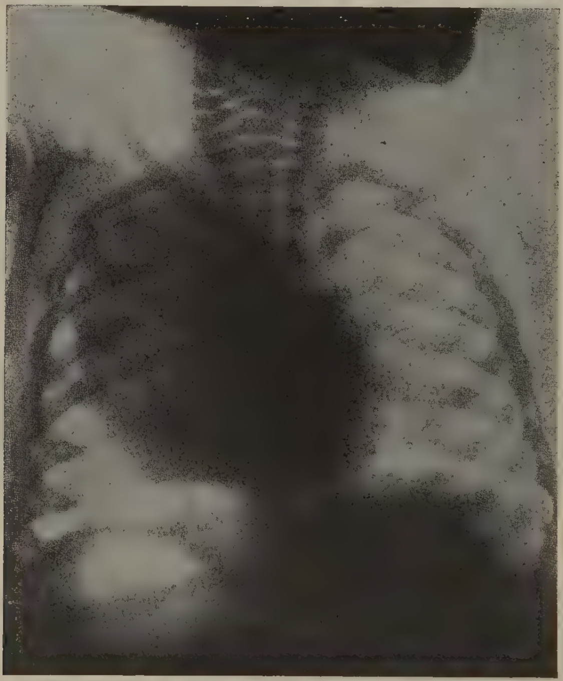

Fig. 284.—Roentgenogram of ganglioneuroma of chest in a boy aged 2½ years. (Stout.[16])

Abdominal Sympathetic.—In the abdomen the tumors have arisen from the celiac or semilunar ganglion, from the adrenal plexus, or from the abdominal or lumbar sympathetic trunk itself. Such tumors have been reported by Busse[20] in a four year old male child; by Beneke[21] in a 10 year old girl; by Ohse[22] in a boy aged five years; and by Braun.[23] All of these tumors were situated on the left side. Peters[2] reported a ganglioneuroma arising from the right abdominal sympathetic trunk in a boy aged 3¼ years. Macnaughton Jones[24] successfully removed a ganglioneuroma of the mesentery of a girl aged 18 years. The tumor had been present since the age of five years, and in the two months preceding operation had increased considerably in size. It contained areas of indifferent, embryonic tissue. In Busse's[20] case, loss of sphincter control of the bladder and rectum, and paralysis of the muscles of the legs had been present since the age of one year. The tumor at operation was found to extend from the diaphragm to the crest of the ilium; it was so broadly attached that removal was done piecemeal and incompletely. Recovery from the operation was not followed by improvement of the paralytic symptoms, which were believed to be due to pressure changes. When seen five years later, the child was apparently well and sphincter control was normal, although function had not returned to the involved leg muscles. In Ohse's[22] case, the tumor, which measured 15 by 13 by 9 cm., was removed surgically, but operation was followed by collapse and death, the latter ascribed to status thymolymphaticus. In Braun's[23] case, the abdomen had been prominent since birth. The tumor was so firmly united to the aorta that the wall of the latter was cut in the removal of the tumor. Suture of the aorta was followed by recovery. The tumor contained young, supposedly proliferating cells, in addition to the characteristic, well differentiated nerve fibers and ganglion cells of ganglioneuroma. Death due to peritonitis followed removal of the tumor reported by Beneke.[21] Peters[2] tumor, successfully removed surgically, was the largest of the group, measuring 20 by 40 cm. and weighing 6 kg. It contained small groups of undifferentiated cells which were not believed to be actively proliferating.

Adrenal.—Ganglioneuromas originating in the adrenal have been described by Fabris,[25] in a 4 year old girl; by Oberndorfer,[26] in a 12 year old girl; and by Hook,[27] in a boy aged 14 years. The first two of these were left sided, the third right.

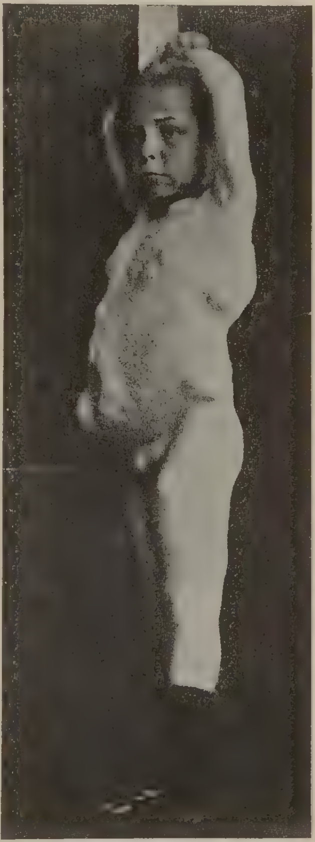

Fig. 285.—Multiple ganglioneuromas of skin; girl aged 11 years. (Knauss.[29])

Pelvic Tumors.—The literature contains four cases of pelvic ganglioneuroma, all in adults. Roman,[28] at the 1924 meeting of the American Association of Pathologists, and Bacteriologists, presented the tumor from which Figs. 279, 280 and 281 come. This tumor filled the pelvis of a child aged three years and extended to the diaphragm; it was believed to have begun in the pelvis. In addition to the differentiated tissues illustrated, it contained areas of younger neurogenic tissue, but this was not considered to be malignant neuroblastomatous tissue.

Peripheral Nerves.—The most striking examples of the tumor under discussion are the two cases of multiple subcutaneous ganglioneuroma in children reported by Knauss[29] and by Kredel and Beneke.[30] In the first of these cases, a girl aged eight years when first coming under observation, multiple small nodules began to make themselves evident beneath the skin when the child was three years old. These increased slowly in size and in number, the larger ones reaching the size of an orange. One of the larger tumors removed when the child was eight years old was considered a neurofibroma. When seen three years later, at the age of 11 years, 63 nodules could be counted beneath the skin (Fig. 285). Several smaller and larger ones removed at this time were composed of medullated and non-medullated nerve fibers and typical ganglion cells of the sympathetic type. Many of the latter contained Nissl bodies, and many were degenerated. No connection with nerve trunks could be detected by palpation, seen at operation, or determined by gross and microscopic study of the tumors removed. Knauss concluded that the tumors had developed from the sympathetic system elements which accompany the blood and lymph vessels. In Kredel and Beneke's case, a small subcutaneous nodule of the neck was noted when the girl was three months old. This increased slowly in size and many others appeared; when the child was seen at the age of five years, 160 tumors could be counted. Tumors removed for study were composed of medullated and non-medullated nerve fibers with well developed sheaths. Typical ganglion cells were present. There was some evidence of infiltrative growth at the periphery, but the tumors were considered histologically benign.

Statistical Summary of Ganglioneuroma.—The most recent and complete tabulation of ganglioneuromas is that of Brunner,[19] who lists 51 without his own. His table, however, requires certain corrections because he has included a number of metastasizing tumors which should be placed in the intermediate group. We have also found a few tumors which he did not include. In the following summary tumors occurring at 16 years of age or under are considered tumors of children.

I. Ganglioneuroma of Brain and Cranial Nerves.—Brunner gives eight cases. To these are to be added de Josselin de Jong's[8] ganglioneuroma of the infra-orbital nerve, Robertson's[7] case of ganglioneuroma of the third ventricle, and our ganglioneuromatous mass of the scalp, all in children and described above. To be added also are Pick and Bielschowsky's[6] tumor of the medulla in a 24 year old woman and Krauss' ganglioneuroma of the eyelid.

Total cases, 13. Age: Adult, 6; child, 3; not stated, 4. Sex: Male, 4; female, 4; not stated, 5. Brain, 5 (including one of dura and one of scalp); nerves, 8.

II. Ganglioneuroma of Neck.—To be added to Brunner's seven cases are the following: De Josselin de Jong's[8] case of cerebroma of the neck in an eight months old girl, described above, and a case reported by Homma in a woman aged 59 years.

Total cases, 9. Age: Adult, 3; child, 6. Sex: Male, 4; female, 4; not stated, 1. Side: Right, 3; left, 6. Origin: Misplaced cerebral tissue, 1; vagus nerve, 1; sympathetic system, 7.

III. Ganglioneuroma of Thoracic Sympathetic.—To be added to Brunner's three cases are those of Tschistowitsch,[17] Rosenson[18] and Stout,[16] all in children and described above; Brunner's own case in a 19 year old girl; and Friedrich's[3] case in a woman aged 73 years.

Total cases, 8. Age: Adult, 3; child, 3; not stated, 2. Sex: Male, 1; female, 5; not stated, 2. Side: Right, 3; left, 4; not stated, 1.

IV. Ganglioneuroma of Adrenal.—Brunner lists six cases, of which that reported by Berner[31] should be removed and placed with the tumors of intermediate type.

Total cases, 5. Age: Adult, 2; child, 1; not stated, 2. Sex, Male, 1; female, 2; not stated, 2. Side: Right, 0; left, 3; not stated, 2.

V. Ganglioneuroma of Abdominal and Pelvic Sympathetics.—Brunner tabulated 21 cases. Of these four should be removed and placed in the intermediate group. To the seventeen remaining cases should be added those of Peters,[2] Macnaughton Jones,[24] and Roman,[28] described above.

Total cases, 20. Age: Adult, 11; child, 7; not stated, 2. Sex: Male, 6; female, 12; not stated, 2. Side: Right, 2; left, 13; median, 2; not stated, or side of origin not to be determined because of the size of the tumor, 3.

VI. Ganglioneuroma of Peripheral Nerves.—Brunner gives six cases. In the two cases credited to Verocay, the tumors did not contain ganglion cells and formed the basis of this writer's introduction of the term neurinoma; Verocay also accepted as a neurinoma the tumor reported by Posthumus as a neurofibroma and included by Brunner among the ganglioneuromas.

Total cases, 3. Age: Adult, 1; child, 2. Sex: Male, 1; female, 2. The two cases in children were multiple and have been described above. The adult case is that of Hagenbach;[32] a small tumor was attached to the capsule of the left knee.

Summary: Total cases, 58. Age: Adult, 26; child, 22; not stated, 10. Sex: Male, 17; female, 28; not stated, 12. Side involved (16 cases of ganglioneuroma of brain and cranial nerves and peripheral nerves being excluded): Right, 8; left, 26; mediar 2; not stated, or side of origin not to be determined because of size of tumor, 6.

Evident from the above is the preponderance of females over males and the much greater frequency of tumors of the left side. One other point is to be borne in mind. While half of the tumors are given as occuring above 16 years of age, the tumor is probably always congenital or the result of embryonic maldevelopment, and in many of the adult cases evidence of the presence of the tumor had existed for years; in most of the other adult cases the tumor was a chance necropsy finding.

Neuroblastoma.—Before taking up the intermediate ganglioneuromas, it is perhaps advisable to consider next the tumors composed of undifferentiated sympathetic cells, since the establishment of the derivation of the neuroblastomas from the sympathetic system was the important factor in clarifying our knowledge of the entire group of neurogenous tumors. In the older literature these tumors masquerade as sarcomas of the adrenal. Some of the earlier sarcomas of the liver, kidney and retroperitoneal lymph nodes of children are also certainly neuroblastomas, the primary tumor in the adrenal or sympathetic system being overlooked or its relation to the larger metastatic tumor not being recognized or appreciated. Of some 20 or more sarcomas of the adrenal of children in the older literature, it is impossible to determine just how many were neuroblastomas.

It was a decided step forward in our knowledge of the nature and origin of these tumors when Küster,[33] in 1905, studied two such neoplasms of the adrenal in children and reported them as gliomas. He noted the tendency of the young undifferentiated cells, which in size and morphology were much like lymphocytes, to arrange themselves in rosettes, the center of each cluster being formed by a mass of very fine fibrils. These latter Küster believed to be neuroglia fibrils, although they did not have the characteristic staining reactions of neuroglia, which he supposed to be due to the embryonic character of both cells and fibrils. Lapointe and Lecene,[34] in reporting a tumor of the left adrenal in a 19 months old girl in 1907, followed Küster in accepting the gliomatous nature of the tumor under discussion. Schilder,[35] in 1909, described in detail a tumor derived from the right abdominal sympathetic in a female infant who died at the age of seven days, both adrenals being normal. He again noted the rosettes or "*Markballen*," which be believed to be formed of embryonic glia tissue, which had been misplaced. He did not believe that such structures are formed in the normally developing sympathetic system and he held, therefore, that they could not come from developing neurocytes.

Although the above writers attempted to prove the origin of the tumor from embryonic glia and deserve credit for having helped to establish its neuorgenous character, it is to be noted that as early as 1891 Marchand,[36] from the study of a small tumor of the right adrenal of a girl aged nine years, had already called attention to the similarity of the tumor tissue to that of the developing adrenal and of the likeness of both to the tissue of the normal, embryonic sympathetic system. Furthermore, in describing a ganglioneuromatous tumor of the gasserian ganglion in 1907, Marchand[37] again emphasized the possible origin of such tumors from the embryonic formative tissue of the nervous system, to the extent of suggesting that such tumors might properly be termed neurocytomas. Kretz,[38] in 1902, in a critical review of the tumors of the liver, recognized the relation of certain of the hepatic tumors of children to adrenal tumors and the similarity of the latter to embryonic sympathetic tissue. In 1905, Wiesel,[39] who had devoted considerable study to the embryology of the adrenal, in a reply to Küster's paper of the same year, held that these tumors are not gliomas but are composed of formative cells of the sympathetic system, from which cells the adrenal of the medulla is developed. Our present conception of the nature of these tumors dates from the publication by Wright,[40] of Boston, in 1910, of a paper entitled "Neurocytoma or neuroblastoma, a kind of tumor not generally recognized."

Development of the Sympathetic System and Adrenal Medulla.—Wright's work and its later general acceptance followed embryologic studies which cleared up the development of the sympathetic system and established the relation of the adrenal medulla to the sympathetic. Kohn[41] showed that the peripheral nervous system is derived from neurocytes, cells which still have the neuroepithelial character of the primitive neural tube from which they come. By division these form the sympathogonia, the formative cells of the sympathetic system. The latter are small cells, with deeply stained nuclei only slightly larger than those of small lymphocytes, with indistinct cell bodies, and with a tendency to arrange themselves in the form of balls or rosettes, characteristics which repeat themselves in the neuroblastoma. It is from cells of this type that the embryonic adrenal medulla is formed.

From the undifferentiated sympathogonia two lines of development occur. The first is through the sympathoblasts, cells somewhat larger than the sympathogonia, to the ganglion cells, neurofibrils, and other essential elements of the sympathetic system. The second line is through the phaeochromoblasts, as the differentiating young cells of the adrenal medulla were termed by Poll,[42] to the phaeochromocytes or chromaffin cells of the adrenal medulla and those other chromaffin derivatives of the sympathetic system to which the term paraganglia has been applied; these include, in addition to the adrenal medulla, the carotid gland, Zuckerkandl's organ, and the coccygeal gland. According to Poll the formation of sympathogonia may continue normally to the tenth year of life, a fact probably of some importance in the development of ganglioneuroma, neuroblastoma and the tumors intermediate between these two. Formative cells may apparently lie dormant indefinitely in the chromaffin and sympathetic systems; one frequently sees in the medulla of the apparently normal adrenal groups of small round cells, sometimes considered evidence of lymphocytic infiltration, but which certainly in some cases are undifferentiated sympathogonia. According to Held[43] the neurocytes may also give rise to glial tissue which is independent of the central nervous system.

From the facts outlined above we are today in position to appreciate the position of ganglioneuroma as one extreme and neuroblastoma as the other extreme of a series of tumors all directly related to each other. We can understand, furthermore, the occurrence of tumors of this series not only in the various part of the sympathetic system itself, but also in the adrenal medulla and the other paraganglia. These relationships have been expressed diagrammatically by Landau,[44] from whose diagram the following schema has been adapted:

Sympathetic System	Corresponding Tumors	
Neuroepithelium of neural tube ↓		
Neurocytes of sympathetic system ↓	→ Pure neurocytoma or neuroepithelioma of sympathetic system (not yet described or recognized as such)	
Sympathogonia ↓	→ Neuroblastoma	→ Intermediate ganglioneuroblastoma
Sympathoblasts ↓	→ Sympathoblastoma (pure form not described)	→
Ganglion cells	→ Ganglioneuroma	→ ↕
Peripheral glia cells (Held) ↓	→ Peripheral glioma	→ Ganglioglioneuroma and ganglioglioneuroblastoma
Phaeochromoblasts ↓	→ Phaeochromoblastoma (not described or recognized)	
Phaeochromocytes	→ Chromaffinoma or paraganglioma	

Characteristics of Neuroblastoma.—The neuroblastoma, being composed of embryonic tissue, is a soft, cellular, sarcoma-liked tumor with the characteristics of malignancy. When arising in the medulla of the adrenal it is usually covered by a capsule and does not directly invade the surrounding tissues and organs. When arising elsewhere it is less well delimited and more markedly invasive. It grows rapidly, it frequently undergoes hemorrhage and regressive changes leading to necrosis of large areas of tissue, and it metastasizes early. The metastases occur in the neighboring lymp-nodes, in the liver, and in the bones, especially those of the skull. Microscopically it is composed of small, lymphocyte-like cells of the sympathogonia type, which may be scattered about irregularly in a finely fibrillated matrix and give to the tissue a sarcomatous appearance (Fig. 286), or they may form the characteristic rosettes. In the latter the cells form one or more rows about a central mass of fine fibrils (Fig. 287). In other areas the fibrils may be arranged in bundles, beside which lie the cells, an arrangement also seen in developing sympathetic ganglia or the adrenal medulla. The tumor may be subdivided by fibrous bands of varying width and density. The thin walled blood vessels present in the cellular tissue may be invaded by the tumor.

Most of the reported tumors have arisen in the adrenal medulla; a few, however, have developed in the sympathetic system. The tumor described by Schilder[35] in a female infant seven days old arose in the sympathetic mesial to the right kidney. This tumor contained well differentiated ganglion cells, which Schilder believed to be some of the original normal cells of the ganglion from which the tumor developed, and not newly formed. The tumor also contained chromaffin cells. Anitschkow[45] reported a neuroblastoma of the left abdominal sympathetic

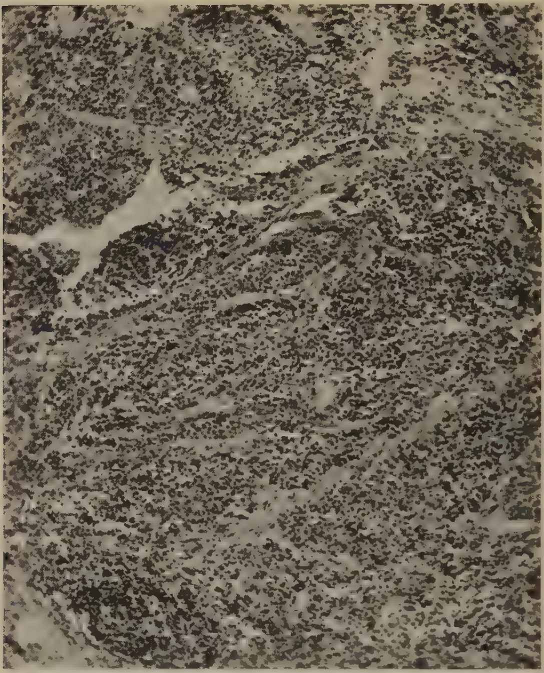

FIG. 286.—Sarcoma-like structure of neuroblastoma; tumor of abdominal sympathetic in a female infant aged 1 month. ×140.

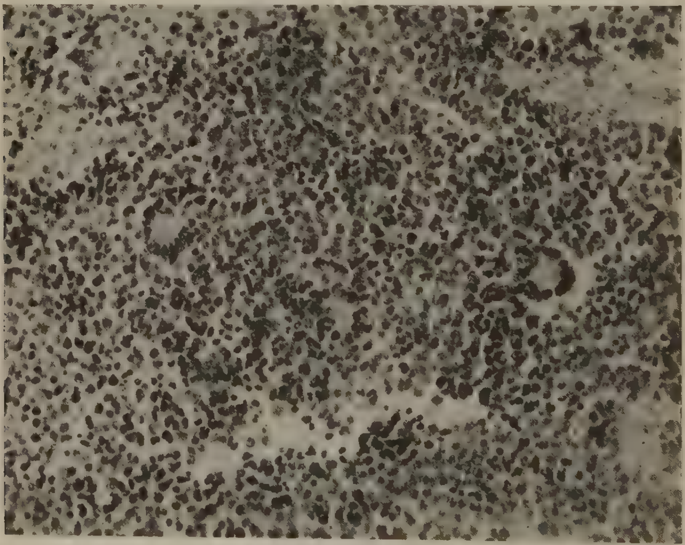

FIG. 287.—Neuroblastoma of abdominal sympathetic; two rosettes embedded in cellular tissue. ×300.

of a girl aged four months. In the personal case from which Figs. 286, 287 and 288 come, a girl aged one month at the time of death, the tumor arose from the left abdominal sympathetic, elements of which were still recognizable in the tumor (Fig. 288). Retroperitoneal neuroblastomas have been reported by Hecht,[46] Wright[40] (Case 4), and Landau;[14] it is probable that these originated in the sympathetic. Stewart[47] reported a neuroblastoma of the cervical sympathetic in a child aged nine years. Benedict[48] described a tumor of the left orbit in a boy of eight years; the tumor apparently did not arise from the retina, but was present beneath the globe, extending from the optic nerve forward almost to the eyelid; the histologic diagnosis was neurocytoma or neuroblastoma. Unusual situations have been the nose, in a case seen by Wolbach (Case 14 of Lehman's[49] tabulation) in a child of three years; and the uterus, supposedly from misplaced sympathetic tissue, as reported by Pick[50] in a girl of 2¼ years. A tumor situated between the rectum and sacrum in a boy aged six years, which contained characteristic rosettes and fibrils, was believed by Alezais and Imbert[51] to have originated in the coccygeal gland.

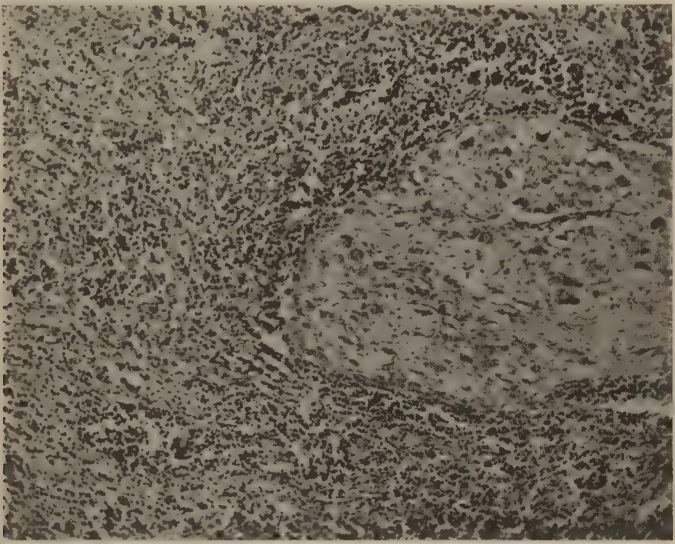

Fig. 288.—Neuroblastoma of abdominal sympathetic; a remnant of sympathetic ganglion is embedded in the invading tumor tissue. ×140.

Age, Sex, and Side Involved.—Herxheimer,[52] who reported a neuroblastoma of the right adrenal in a boy aged 1½ month and made the case the basis of one of the most thorough contributions on the subject, collected 28 cases from the literature previous to 1914, but admitted that some of the older ones were doubtful. All of these tumors were in children, the oldest being aged nine years. The age was stated in 26 of the cases; only eight were over one year old, and only 12 reached an age of over three months. The sex was stated in 20 cases; of these, 13 were females and 7 were males. Twenty-one of 25 cases in which the origin could be established arose in the adrenal, seven times from the left adrenal and nine times from the right; in five of the adrenal cases the tumor was bilateral. Lehman,[49] who reported a neuroblastoma of the right adrenal in a male infant aged 11 months, accepted only 25 cases, including his own, as true neuroblastomas. His tabulation includes the cases of Wahl[53] and Martius,[54] which we shall place in the intermediate group. Omitting these two, the oldest case accepted by Lehman was aged 14 years, this being the adrenal tumor reported by Dunn.[55] Since Lehman's publication, there have been the tumor of the cervical sympathetic reported by Stewart,[47] and of the orbit reported by Benedict,[48] both noted above; and a neuroblastoma of the left adrenal in a boy aged four years, recorded by Wolbach and Morse;[56] to these may be added our case, which has not been previously reported. Wolbach and Morse mention two additional cases, a boy aged seven months and a girl aged two years, in which the diagnosis was made from tissue removed at surgical operation. In Lehman's[49] case the tumor was removed surgically; the child was apparently well 2½ months after the operation. The most striking feature of neuroblastoma, especially in comparison with ganglioneuroma, is the early age at which the tumor occurs; it was present at birth in one of Wright's[46] and in one of Landau's[44] cases, in both of these being bilateral. The only apparent exceptions to the rule of the early occurrence of neuroblastoma are the second of Küster's[33] cases and a case reported by Barnewitz.[57] Although Küster's first case was a typical one in a child, his second tumor was a museum preparation concerning which the data were that it was from an adult. It contained ganglion cells and nerve fibers, as well as undifferentiated tissue, and therefore belongs in the intermediate group. The case reported by Barnewitz was a woman aged 37 years, with a tumor of the right adrenal and metastases in both ovaries and in the apex of one lung; although the author described small cells arranged in rosettes, his illustrations lead to the belief that the tumor was a hypernephroma.

Tumors Intermediate between Ganglioneuroma and Neuroblastoma.— In the discussion which has preceded, it was necessary frequently to refer to tumors which were intermediate between ganglioneuroma and neuroblastoma, in so far as their histologic structure is concerned. It is to the study of these intermediate tumors, as well as to the development of our knowledge of the embryogenesis of the sympathetic system, that we owe our present conception of the entire group of neurogenous tumors. Certain of the intermediate tumors contain both ganglioneuromatous and neuroblastomatous tissues, as well as the successive stages of differentiation of the latter to the former. Certain others contain the elements of ganglioneuroma, and apparently dormant formative tissue. The individual tumors of the group shade off imperceptibly into each other and into pure ganglioneuromas and neuroblastomas which form the extremes of the series.

For the tumors which contain both well differentiated ganglion cells and undifferentiated sympathogonia Robertson,[58] in 1915, proposed the name ganglioneuroblastoma. Lehman[49] deprecated the introduction of a new term, upon the ground that all gradations occur and that it is, therefore, difficult or impossible sharply to delimit an intermediate or mixed group of tumors from the ganglioneuromas and neuroblastomas at either extreme of the series. We may agree with Lehman that limitation and characterization are difficult, but the presence of proliferating formative tissue in a tumor composed predominatingly of differentiated ganglion cells and nerve fibers or of the latter elements in a tumor composed largely of neuroblastomatous tissue is so important for an understanding of the genesis and clinical characters of these tumors that a name which calls attention to the mixed condition of certain of the neoplasms is not amiss. They take an intermediate position not only in their histologic structure but also in regard to the age at which they may occur and to their tendency to form metastases. The formation of metastases with recognizable ganglion cells raises a question as to whether ganglion cells may proliferate and metastasize as such or whether they must arise by differentiation from transported neuroblastic elements. The presence of apparently dormant sympathogonia and sympathoblastic tissue in certain tumors may help to explain the sudden development of malignancy in tumors previously clinically benign, if we grant that undifferentiated tissue which has lain dormant for years may take on a sudden accession of proliferative activity.

Ganglioneuroma with Undifferentiated Areas.—Certain of the tumors of children already included above with the benign ganglioneuromas contained a variable amount of undifferentiated tissue. Peters[2] did not believe that the small amount of this tissue present in his tumor was actively proliferating, but that it showed only evidences of differentiation, indicating a still active formation of ganglion cells. Freund's[14] tumor contained small, alveolar areas of lymphocyte-like cells with some larger cells of the sympathoblast type; fine fibrils, such as occur in neuroblastoma, were present in these areas. She believed this tissue to be glia, because she could not trace the further stages from sympathoblasts to ganglion cells. A tumor of the left abdominal sympathetic in a woman aged 20 years, reported by Wegelin,[5] contained groups of small, incompletely differentiated ganglion cells and sympathoblasts. Küster's[33] tumor from an adult, referred to above, was of similar character. von Fischer,[59] in 1922, reported a tumor of the left cervical sympathetic of a still-born child; it contained areas of sympathogonia with the characteristic fibrillated rosette arrangement, other areas of sympathoblasts lying in a ground-work of neurofibrils, and a few ganglion cells which lay in or near the groups of sympathoblasts. This tumor evidently was an immature ganglioneuroma, in which active proliferation was still in progress and which might have led in time, if the child had lived, to the formation of a well differentiated, typical ganglioneuroma. Tumors like the above probably do not require separate classification, but they are included here as representatives of the link which unites the more actively proliferating tumors with the ripe ganglioneuromas.

Ganglioneuroma with Proliferating Undifferentiated Tissue.—In Macnaughton Jones'[24] tumor, included above with the ganglioneuromas, the greater part of the tissue was of the kind characteristic of ganglioneuroma, but the undifferentiated tissue present was such, both in amount and character, as to indicate that this tissue was actively proliferating. Furthermore, the clinical history of quiescence for many years, with decided increase in size during a period of two months before operation, also pointed to recently increased activity on the part of the tumor.

Ganglioneuroma with Proliferating Ganglionic Tissue.—Beneke,[21] in 1901, described a tumor of the abdomen in a girl aged 10 years. It was as large as a man's head and arose apparently from the celiac ganglion. In its general structure it was a typical ganglioneuroma; it contained medullated and non-medullated nerve fibers with Schwann sheaths, and numerous ganglion cells. Many of the latter were multinucleated and appeared to be actively multiplying, although their ganglionic character was readily recognizable. The neighboring lymph-nodes contained aggregations of similar proliferating ganglion cells, a condition interpreted as evidence of malignant proliferation of ganglion cells themselves. Miller,[60] in 1908, reported a small tumor which arose from the left celiac ganglion in a girl aged 16 years and who had committed suicide, the tumor being an accidental necropsy finding. The tumor was composed of nerve fibers and ganglion cells, as well as cellular areas which were termed lymphoid tissue. The neighboring slightly enlarged lymph-nodes consisted largely of similar cellular tissue, together with ganglion cells and axis cylinders in small numbers. Brossok,[61] in 1911, described a tumor the size of a child's head which had replaced the right adrenal of a girl aged 11 years and which had invaded the liver by continuity. The tumor contained well differentiated ganglion cells, as well as multinucleated and small mononucleated forms which were believed to be actively proliferating. A large central necrotic area was bounded in places by cellular tissue composed of round cells. The liver and lymph-node metastases were made up of similar cellular tissue, in which ganglion cells were scattered. In the last two cases it is difficult to determine whether the tumors illustrate actual metastasis of ganglion cells or metastasis of formative tissue which had partially differentiated into ganglion cells. Sommerfeldt,[62] who reported a ganglioneuroma of the cervical sympathetic in a woman of 36 years, denied the proliferative capacity of ganglion cells and doubted that the supposed metastases in Beneke's and Miller's cases were true secondary tumors. He believed that they were probably the result of the same phenomenon of misplacement of embryonic sympathetic tissue which was responsible for the main tumor. Berner,[31] in 1922, reported a tumor of the left adrenal of a girl aged 4½ years, which he thought answered Sommerfeldt's objections. The tumor measured 13 by 10 by 8 cm. and was made up of bundles of non-medullated nerve fibers with sheath cells, axis cylinders without sheaths, and groups of well differentiated ganglion cells some of which were multinucleated. There were no young formative cells and the ganglionic character of even the youngest cells could be readily recognized. The neighboring lymph nodes, which were small, contained areas composed of nerve fibers and ganglion cells. Berner's case is the only one in the entire group of adrenal ganglioneuromas and neuroblastomas in which there was anything clinically suggestive of Addison's disease; the patient had well marked melanodermia, but there was no pigmentation of the buccal mucosa. While we can not exclude the derivation of the ganglion cells of the metastases of Miller's and Brossok's tumors from transported undifferentiated tissue, the tumors of Beneke and of Berner furnish rather conclusive evidence that sympathetic tissue which has already reached such a stage of differentiation as to permit its recognition as ganglionic tissue may metastasize as such.

Neuroblastoma with Areas of Ganglioneuroma.—Tumors of mixed type with the metastasis of cellular neuroblastomatous tissue are the most numerous of the intermediate ones and form the final stage in the transition from ganglioneuroma to neuroblastoma. One peculiarity of some of them is that the two types of tissue need not be intermingled; frequently one part of the tumor is characteristically ganglioneuromatous, whereas another portion may be definitely neuroblastomatous. In the first of the two cases reported by Robertson[58] in 1915, the tumor, apparently a fibromyoma of the cervix uteri, formed a large mass in the pelvis of a girl aged 16 years, which interfered with the delivery of her child and necessitated cesarean section. Upon operative removal five weeks later, the tumor was found to consist of a mass 9 cm. in diameter, closely adherent to the anterior surface of the sacrum, with two attached, firm masses each 2 cm. in diameter. Removal was followed by local recurrence. The smaller masses were typical ganglioneuroma, with ganglion cells and non-medullated nerve fibers. The larger mass was a typical neuroblastoma, composed of sympathogonia and sympathoblasts, which in places formed rosettes. Martius[54] studied a tumor of the right side of the neck of a boy aged 2½ years. The tumor had interfered with respiration by pressure on the trachea. At operation there was removed a large encapsulated mass which was adherent to the thyroid, from which the tumor was believed to have originated. Collapse and death followed the operation. At necropsy smaller nodular masses were still present in the right side of the neck, one of which arose from the sympathetic trunk. The smaller masses were ganglioneuroma, the larger tumor neuroblastoma. A most interesting tumor is that which Wahl[53] made the basis of the most complete contribution in the English language to the literature of the neoplasms of sympathetic system origin. The tumor, which occurred in a girl 2½ years of age, arose from the left adrenal. It consisted of an inner, firmer ganglioneuromatous portion, and a larger, outer, softer neuroblastomatous part. Isolated small masses of chromaffin tissue were present throughout the tumor, being most numerous in the densest part. Neuroblastomatous metastases, which contained no ganglion or chromaffin cells, were present in the liver, lymph-nodes and kidneys.

Dunn[55] reported a tumor of the left adrenal in a boy aged 4½ years, operative removal having been attempted under the belief that the condition was a renal neoplasm. The adrenal tumor measured 9 by 8 cm. There were numerous metastases in the lymph-nodes, pleura, peritoneum, ribs and skull. The main tumor contained older, denser portions with the characteristic structure of ganglioneuroma, and softer areas of typical neuroblastoma. The metastases consisted of the latter kind of tissue. In Robertson's[58] second case, a tumor of the right adrenal of a girl aged five years, removal of the tumor was followed by orbital metastasis and death. The tumor was composed of ganglioneuromatous and neuroblastomatous areas intermingled with each other. Jakobsthal, in discussion of Riesel's[63] presentation of a specimen from Braun's[23] tumor, referred to a large ganglioneuroma of the celiac ganglion, seen by him in a child aged eight years. Metastases were present in the liver. The primary tumor contained cellular areas which Jakobsthal believed to be gliomatous, but which were probably neuroblastomatous. Glomset's[64] tumor of the right adrenal of a male child aged two years was composed of cellular neuroblastomatous tissue with typical rosettes, and contained a few multinucleated ganglion cells.

Dunn's tumor, that of Robertson's second case, Jakobsthal's and Glomset's are examples of neoplasms in which the most and the least differentiated forms of sympathetic neurogenous tissue are intimately intermingled with each other. Jaffé[65] has reported a similar tumor, measuring 22 by 20 by 8 cm., of the left adrenal of a man 31 years old. The tumors of this kind show all stages of transition from sympathogonia to ganglion cells. The tumor of Robertson's first case, and those reported by Martius and Wahl differ somewhat in that the gangliomatous and neuroblastomatous parts are more or less distinct from each other. In such tumors the transition stages from sympathogonia to ganglion cells are less well seen. What happened in these neoplasms was probably the sudden accession of growth upon the part of localized areas of undifferentiated tissue in a tumor, the greater part of which had completed its differentiation to ganglion cells. von Fischer[59] discussed the possibility of what one might, in a way, consider the spontaneous "healing" of a tumor like that of Peters,[2] which still contains, at the time it comes to examination, undifferentiated tissue. Progressive differentiation might transform the tumor into a harmless, benign, ganglioneuroma, which would remain harmless if all the formative tissue completed its differentiation. Whether, in a given tumor which begins, as all of them must, in formative sympathetic tissue, the result will be a malignant neuroblastoma, a benign ganglioneuroma, or a benign or malignant ganglioneuroblastoma, will depend upon the continuous proliferation of the undifferentiated tissue, upon its progressive and complete differentiation, or upon its partial and incomplete differentiation. In the last case, we have the further possibility that the undifferentiated tissue may remain dormant, or that it may suddenly begin to proliferate wildly.

Statistical Summary of Intermediate Ganglioneuroblastomas.—In the discussion above of the intermediate tumors, reference has been made to the following neoplasms which were not included in the summary of ganglioneuromas given on page 752: Küster's second case, Wegelin, v. Fischer, Miller, Brossok, Berner, Robertson's two cases, Martius, Wahl, Dunn, Jakobsthal, Glomset, and Jaffé. The data in regard to these may be summarized as follows: Total cases, 14, Age: Adult, 3; child, 11: Sex: Male, 4; female, 7; not stated, 3. This summary reveals certain interesting facts, namely, a preponderance of children over adults, a characteristic which becomes even more marked in the neuroblastomas; the same preponderance of females over males that occurs with both ganglioneuroma and neuroblastoma; and the same preponderance of left sided involvement over right sided that holds for ganglioneuroma. In the intermediate tumors of children the age varied from birth to 16 years, being distributed as follows: First five years of life, six cases; second five years, one case, third five years, one case; fourth five years (16th year), two cases.

Classification of Intermediate Ganglioneuroblastomas.—Attention has been called above to the difficulty of drawing a sharp line of distinction between ganglioneuroma and certain of the intermediate tumors on the one hand, and between neuroblastoma and certain other tumors of mixed composition on the other hand. Because the intermediate tumors are so important for an understanding of the entire group, it appears advisable to attempt to place them in a separate subgroup, for which Robertson's[58] proposed name of ganglioneuroblastoma may be accepted. If such a scheme is followed, ganglioneuroma should be reserved for tumors which contain only ganglion cells and nerve fibers and no undifferentiated tissue, and neuroblastoma for neoplasms which contain only formative tissue and no ganglion cells. Within the subgroup of intermediate tumors or ganglioneuroblastomas there are, however, distinct variations, which suggest the advisability of still further classification. Transition stages and tumors composed of different parts with different structure without transition, make finer classification difficult. Such a further division of the intermediate tumors has been attempted by v. Fischer.[59] He himself admitted the difficulty encountered in fitting certain tumors into the scheme, but the attempt is of some value because it proposes names for certain more striking characteristics. von Fischer's classification, slightly modified, is as follows:

I. Completely Differentiated:

1. Ganglioneuroma Simplex.—Completely differentiated, without formative tissue. Clinically and histologically benign.

II. Partly Differentiated (Intermediate Forms):

2. Ganglioneuroma Immaturum.—Younger formative cells, which do not appear to be actively proliferating but show the stages of differentiation to ganglion cells. Benign.

3. Ganglioneuroma Imperfectum.—There is active formation of undifferentiated tissue, but differentiation keeps pace with new formation. The distinction between 2 and 3 is not sharp, and it might be better to combine these into a single subgroup.

4. Proliferating Ganglioneuroma.—Formative tissue is present, as are also ganglion cells. The latter show greater activity than the former. The metastases may contain ganglion cells and nerve fibers.

5. Neuroblastoma Gangliocellulare.—Transition stages from formative cells to ganglion cells are present, but the ganglion cells themselves show evidence of proliferative activity. The formative tissue is also active and may lead to metastasis of neuroblastomatous tissue. The dividing line between 4 and 5 is again indefinite and it might be better to combine these into a single subgroup.

III. Completely Undifferentiated.

6. Neuroblastoma Simplex.—Composed only of actively proliferating formative tissue, whose differentiation does not proceed far enough to lead to the formation of typical ganglion cells. Since two kinds of indifferent cells are recognized, it is theoretically possible to subdivide this group further into:

(*A*) Sympathoblastoma.—Composed of sympathoblasts, cells of about the size of large lymphocytes, with vesicular nuclei; the mother cells of the ganglion cells.

(*B*) Sympathogonioma.—Proposed by Kohler[66] for tumors composed of cells of the youngest type, i.e., sympathogonia. Pure forms of sympathoblastoma and of sympathogonioma probably do not occur. Most neuroblastomas contain chiefly sympathogonia, but with an admixture of sympathoblasts.

Chromaffinoma.—Since the sympathetic system gives rise to the chromaffin tissue of the adrenal medulla and of the other paraganglia, there is given the theoretical possibility of the occurrence of tumors composed of chromaffin cells; such neoplasms would be closely related genetically to the neuroblastomas and ganglioneuromas. If composed of the young, undifferentiated chromaffin cells, the phaeochromoblasts of Poll,[42] such a tumor might be termed phaeochromoblastoma. Tumors of this kind have not been reported, possibly because it is not possible to recognize the phaeochromoblasts as such or to distinguish them from sympathogonia. It is theoretically conceivable that some of the reported neuroblastomas may be phaeochromoblastomas, but that they actually are can not be determined unless the tumor, by differentiation, forms recognizable chromaffin tissue. As a matter of fact, Wahl's[53] neuroblastoma illustrates both possible lines of differentiation of neuroblastomatous tissue and contained both recognizable ganglionic and chromaffin tissues.

Phaeochromocytoma.—For neoplasms containing differentiated chromaffin tissue, Landau[44] proposed the name phaeochromocytoma, which is definitive but unwieldy. Chromaffinoma or chromaffin tumor appears to be preferred by most writers. Hyperplasia of the chromaffin tissue of the adrenal medulla is apparently fairly frequent, but true tumors are rare. All of those which have been reported have been in adults. Some of those of the adrenal (Suzuki's[67] first case, Hedinger's[68] case) reached a diameter of 10 cm. These large tumors were centrally degenerated and cystic. All have been encapsulated or sharply delimited and apparently benign. The cells which gave the chrome reaction were polyhedral, closely placed without intervening reticulum, and formed alveoli composed of six to ten cells each, the alveoli being separated by fibrous tissue. Hedinger's tumor and those of the first and third cases reported by Suzuki contained a small amount of tissue made up of small, lymphocyte-like cells, which each of these authors believed to be undifferentiated formative cells. In its peripheral parts Hedinger's tumor contained a few ganglion cells and nerve fibers; these findings are probably to be interpreted, as in Wahl's case, as the result of differentiation of embryonic sympathetic tissue to both nervous and chromaffin elements.

Stangl[70] described a chromaffin tumor of Zuckerkandl's organ, and Mönckeberg[71] two of the carotid gland. These also occurred in adults. Probably most of the so-called endotheliomas and peritheliomas of the carotid and coccygeal glands have been chromaffinomas, although this point can not be certainly determined in those examples in which the chrome reaction was not done. A pea-sized chromaffin nodule of the right adrenal of a man aged 35 years, who died of generalized tuberculosis and whose skin was pigmented, was termed by Laignel-Lavastine and Aubertin[72] an adenoma of the adrenal medulla. The acceptance by certain French pathologists of epithelial glandular tumors of the adrenal medulla leaves one in doubt as to the exact nature of this tumor. Herxheimer[52] placed fifteen tumors reported previous to 1914 in the chromaffinoma group, all of which were in adults and all were benign.

Chromaffinoma of the Kidney.—The most interesting tumor of the chromaffinoma group and one which occurred in a child is that reported by de Vecchi[73] in 1905. In a male child which died at the age of one year and seven months, the pelvis of each kidney was occupied by reddish, fleshy tumor tissue which grew up into the calyces and surrounded the papillæ, but which had not invaded the renal tissue and had not caused hydronephrosis. According to the description of de Vecchi, who considered the tumor a sarcoma, it was composed of masses of small rounded cells, of about the size of lymphocytes, with no intervening supporting tissue. The clumps or groups of cells of this type were separated from each other by bands of fibrous stroma. In its peripheral portions the tumor tissue contained small groups or lobules of larger ovoid cells which gave the chrome reaction and which de Vecchi recognized as chromaffin tissue. The author interpreted the condition as a primary bilateral sarcoma of the pelvis of the kidney, in which misplaced chromaffin tissue had been included, and believed that he was dealing with an unusual type of the common mixed tumor of the kidney. His illustrations show a decidedly alveolar arrangement of the tissue which he believed to be sarcomatous. In view of the knowledge of the histology of chromaffinoma derived from the tumors reported at a later date by Suzuki and Hedinger, it appears more probable that de Vecchi was dealing with a pure chromaffin tumor, of bilateral origin, due to misplacement of embryonic parasympathetic tissue. If this is the correct interpretation, this tumor would come nearest to answering the description of the theoretical phaeochromoblastoma. It is, furthermore, the only chromaffin tumor which we have been able to find in childhood.

Paraganglioma.—In connection with tumors of the adrenal medulla and of the other paraganglia of sympathetic origin, brief mention should be made, for the sake of completeness, of the belief of French pathologists that paraganglionic adrenal tissue may give rise to true epithelial neoplasms. Peyron[74] has devoted an extensive article to such tumors, for which he proposed the name paraganglioma. He admitted that they are extremely rare, but described several from lower animals and a few from man. All were benign, except one in the horse. His descriptions and numerous illustrations indicate a decidedly alveolar, epithelial character, which is sometimes distinctly glandular, but leave one wondering whether he may not have been dealing with adenoma-like misplacements of adrenal cortical tissue into the medulla. One not infrequently sees in the apparently normal adrenal medulla of both children and adults cords and gland-like aggregates of cells of distinctly epithelial character, and in no way similar to the cortical cells. The formation of these structures is not accounted for by the purely sympathetic tissue origin of the adrenal medulla, unless we conclude that such cells have retained their primitive neuroepithelial characters or are comparable to ependyma. Perhaps some of the more characteristically epithelial tumors described by Peyron may come from such elements. The term paraganglioma, as used by the French and Germans, relates to two kinds of tumors which are morphologically quite distinct. As used by most German pathologists, the paraganglioma is a non-epithelial tumor, probably of embryonic sympathetic tissue origin, which may occur in the paraganglionic structures, the adrenal medulla, carotid and coccygeal glands and Zuckerkandl's organ.

Neuroglioma of the Retina.—Table 2 (page 707), based on Steffen's[75] compilation of malignant tumors of childhood, shows that tumors of the eye rank second to those of the kidney and adrenal. Since practically all of these tumors are of the type to which the term neuroglioma of the retina is usually applied, their relative frequency alone gives to them great importance among the tumors of the early years of life. They are, moreover, tumors which belong characteristically to the childhood period; according to Greeff,[76] glioma of the retina has never been known to arise after the twelfth year of life. Berrisford,[79] in 1916, brought the statistics of Moorsfields Hospital, London, down to that date from 1871. There had been 153 cases of glioma retinae, of which none occurred after the age of seven years. The incidence increased gradually from birth to the second year of life, and receded from this point to only two cases during the seventh year. In 56 cases the tumor was first noted during the first year, and in 26 cases it first manifested itself during the second year of life. One hundred and thirty-one cases occurred in 1,259,452 patients, a frequency of 1 in 9614 or 0.01 per cent. Of 792 collected cases, 398 were males (50 per cent.), 361 (46 per cent.), were females, the sex not being stated in 33. The tumor was bilateral in 25 per cent.

In spite of its importance, both from the standpoint of its frequency and of its effect upon the child, the tumor has received scant attention in the text-books of special pathology or in the general pathologic literature; Kaufmann[78] dismisses the subject with a single paragraph in a footnote. It might be supposed that our knowledge of the nature and origin of the neoplasm is quite definite and that there are no controversial points which still require elucidation. That such is not the case is evident from the names which have been applied to the tumor: Glioma, neuroglioma, gliosarcoma, neuroepithelioma, neuroblastoma, encephaloid, dictyoma, angiosarcoma, perithelioma, round cell sarcoma. This varied nomenclature indicates a lack of unanimity of opinion in regard to the nature of the tumor, which is borne out by the relatively scanty literature on the subject. Since it may closely resemble neuroblastoma, and since its frequent congenital occurrence indicates its origin from embryonic tissue, consideration will be given to it at this place, in connection with the neurogenous tumors described above.

Development of the Retina.—Embryogenetically the retina is the result of the evagination of the neuroepithelium of the primitive forebrain, a process which results in the formation of the optic vesicle. Invagination of the anterior half of the vesicle folds this portion back upon the posterior half, the latter giving rise to the pigmentary layer, the former to the specific structures of the retina. The retina, therefore, is to be looked upon as ectodermal in origin and as a highly differentiated part of the central nervous system. We have seen above how complicated is the process of differentiation through which the primitive tissue derived from the embryonic nervous system passes to form the sympathetic system. The neuroepithelium of the retina likewise forms a variety of structural elements, some of which, like the ganglion cell layer, the nerve fibril layer and the dendrites of the molecular layers take on the characteristics of nervous tissue, whereas others, like the rods and cones and their associated granular layers, are more epithelial in character. The occurrence of true neuroglia in the normal retina appears quite doubtful, and the tumors of the retina can not, therefore, be accepted off-hand as gliomas; the presence of glial tissue in these tumors, if it is present, requires explanation.

Characteristics of Retinal Tumor.—The neoplasm under consideration may be already present at birth, manifesting itself by fixation, irregularity of outline and haziness of the pupil. Its frequent occurrence in more than one member of a family is suggestive of a familial or hereditary tendency. The tumor is primarily bilateral in a relatively high proportion of cases; in 18 per cent., according to Hirschberg,[79] in 20 per cent. according to Ziegler,[80] in 25 per cent. according to Berrisford,[76] and in 26 per cent. according to Parsons.[81] It arises usually from the fundal portion of the retina, but may take its origin from the pars ciliaris, as in the case reported by Emanuel.[82] It soon fills the chambers of the eye and makes its appearance externally, forming a protruding, fungoid, soft, pale, largely necrotic mass, characteristics which gave to the tumor its names of encephaloid or "*Markschwamm.*" It grows along the optic nerve and metastasizes to the brain and to the bones of the skull and face. Secondary tumors may occur throughout the entire skeleton without brain involvement, as in the case reported by Roman.[83] Metastases may occur in the cervical lymph nodes and in the liver. The relative distribution of metastases in 155 cases was given by Wintersteiner[84] as follows: Brain and membranes, 43; skull and bones of face, 40; lymph-nodes, 36; parotid, 9; skeletal bones, 9; liver, 7; spinal cord and membranes, 5; kidneys, 2; ovaries, 2; lung 1; spleen 1. Clinically it is a highly malignant neoplasm, which requires early recognition and early operative removal if the life of the child is to be saved. Roentgen-ray therapy does not appear to be very hopeful; in seventeen reported cases collected by Jacoby,[85] who reported three cases of his own treated by radiation, temporary good results were obtained in only three.

Histology.—The tumor is cellular, being composed of closely placed cells with indistinct outlines and small, deeply stained nuclei about the size and appearance of those of small lymphocytes. The cells lie in a finely granular or finely fibrillated, faintly staining ground substance. Fine strands of connective tissue carry thin walled blood vessels. It is this general appearance of the tumor issue, influenced perhaps by the nervous origin of the retina, which has given the name glioma or neuroglioma; as a matter of fact, the tissue does not give the specific staining reactions of neuroglia by the usually applied methods. A close similarity to the undifferentiated retina of the third fetal month has been noted. Selenkowski[86] described the presence of ganglion cells and of embryonic cells, some of which he believed might be the precursors of ganglion cells. Greeff[76] also saw ganglion cells and proposed the name neuroglioma ganglionare for the tumor. At times the cells take on a rosette-like arrangement strikingly like that of neuroblastoma. At other times they may form alveoli which suggest an epitheliomatous character.

Frequently the cells are radially arranged about the blood-vessels, hence the terms perithelioma and angiosarcoma.

Origin and Nature of the Tumor.—The greatest uncertainity and controversy relate to the peculiar rosettes which may be present. If their origin could be definitely established, our knowledge of the nature of the tumor would be more exact. Flexner[87] apparently first called attention to them in 1891 and compared the cells which compose them with the cells of the ependyma of the nervous system. He proposed the name neuroepithelioma, suggesting an origin from undifferentiated neural epithelium. Wintersteiner,[84] who devoted an extensive monograph to the subject in 1897, accepted the term neuroepithelioma and considered the rosettes the characteristic elements of the tumor. He, however, derived the tumor cells from the rod and cone and outer granular layers, which he believed retain their epithelial characters. Here, then, are two observers, both of whom accept the name neuroepithelioma, but one derives the tumor from primitive neural epithelium, the other from more highly differentiated elements of the retina. Steinhaus[88] believed that the rosettes come from misplaced embryonic neuroepithelium, which may differentiate to both glia and ganglion cells. Opposed to the above are a larger number of observers who explain the rosettes as the result of mechanical factors. Ginsberg[89] believed them to be due to shrinkage of the retina and to separation of the layers. Pusey[90] observed similar structures, which he believed to be formed by folding of the retina, in inflammatory conditions. Wehrli,[91] who accepted the gliomatous character of the neoplasm, likewise ascribed the rosettes in part to separation and infolding, and in part to the tendency of the neurogliomatous tissue to arrange itself about the blood vessels. It is apparent from the above how widely divergent are the opinions which are fundamental for an understanding of the nature of the tumor.

Neuroglioma or Neuroblastoma?—It is to be noted that the above work antedates our present knowledge of the neuroblastoma of the sympathetic and adrenal. Bernhard Fischer,[92] with this information in mind, believed the retinal tumor to be identical with the neuroblastoma. He conceived it to be derived from primitive neuroblasts, which may differentiate here, as they do in the adrenal and sympathetic, to glia, ganglion cells, and cells which have the characteristics of retinal cells. More recently again, however, Urra[93] has claimed that by the newest staining methods it is possible to distinguish astrocytes and glia fibers and that the retinal tumor is, therefore, a glioma. He admitted that the younger cells are so undifferentiated that their neuroglial nature can not be determined. The formation of rosettes he explained by the arrangement of younger cells radially about a differentiated astrocyte, between whose fibrils the young cells were said to lie. In view of our present knowledge of the neuroblastomas and of the variety of cellular structures to which they may give rise; in view of the close similarity of the rosettes of neuroblastoma to those of the retinal tumor; in view of the fact that undifferentiated neuroblasts might give rise to ganglion cells, nerve fibrils, and neuroglia, elements which have been described in the retinal tumor; and in view, finally, of the absence of glia in the normal retina and of the difficulty of establishing its presence in the retinal tumor, it appears most reasonable to look upon the latter as a neuroblastoma, a tumor derived from indifferent, embryonic neuroblasts or neurocytes, which have been misplaced during the fetal period of development or have lain dormant and have not completed their normal cycle to form differentiated retinal elements. This conception would group together retinal neuroglioma and neuroblastoma, a grouping which is warranted by the close histologic similarity, by the early congenital origin, and by the tendency to multiple bone metastases common to both neoplasms.

Neuroma.—To tumors of peripheral nerves the term neuroma was generally applied in the older pathologic literature, but a more precise definition of neuroma remained for Virchow[94] to formulate. The latter insisted that only those tumors in which a new formation of nerve fibers had occurred could be considered true neuromas. The knowledge of nerve tumors remained in an unsatisfactory state until the appearance of v. Recklinghausen's[95] important monograph in 1882. He made a detailed study of the multiple tumors, especially of the subcutaneous nerves, which characterize the condition to which his name is attached. He concluded that these tumors do not contain newly formed nerve fibers, but are composed only of fibrous tissue derived from that of the nerve trunks. There followed then a period in which the participation of nerve elements in the formation of tumors of nerves was rather generally denied, and the occurrence of true neuroma appeared doubtful. In 1887 Krause[96] reported three cases of malignant tumor, sarcoma, of peripheral nerves in adults and convinced himself that an increase in the number of nerve fibers had occurred in the cellular tumor tissue. He was unable to decide, however, whether the increased content of nerve fibers was the result merely of an increase in the length of preexisting fibers, brought about by the stimulus of the malignant tumor, or of an actual multiplication of the fibers.* The latter, except through longitudinal division of axis cylinders and independent growth, appeared improbable because of the views then held, which looked upon the axis cylinder as a distinct and continuous outgrowth of the ganglion cell.

Neurinoma.—Later embryologic investigations led certain anatomists (Balfour, Bethe. Schultze, Apathy, and Hertwig,[97] the last named of whom has discussed the subject at length) to accept the peripheral formation of nerve fibers, independent of the ganglionic axons with which the fibers thus formed become united. According to this conception, the cells of the sheath of Schwann are neurogenous in nature and ectodermal in origin, and give rise to peripheral nerve fibers.* In 1910 Verocay[98] investigated a case of multiple tumors of the cranial and peripheral nerves, the condition clinically having been an apparently typical v. Recklinghausen's disease. The tumors in this case, however, were more cellular than the usual neurofibroma. They were composed of bundles of elongated, young, sarcoma-like cells arranged between bands of denser fibrous tissue. In the tumors of the spinal root ganglia, ganglion cells were present, some of which were believed by Verocay to be newly formed. He concluded that the cellular tissue was derived from the cells of the sheath of Schwann, and that it was undifferentiated neurogenic tissue, which had the potentiality of forming glia, ganglion cells and nerve fibers. He likened the condition to a peripheral glioma, although true neuroglia could not be demonstrated in the tissue studied. The similarity of this conception to that which derives the neuroblastoma and the ganglioneuroma from embryonic neurogenic tissue will be recognized. Furthermore, the condition described by Verocay has analogies with the examples of multiple peripheral ganglioneuroma reported by Knauss[29] and by Kredel and Beneke.[30] Verocay's designation of neurinoma for such more cellular tumors of peripheral nerves, together with his belief that they are neurogenous in origin, has been accepted by a number of later writers, some of whom go so far as to believe that all the v. Recklinghausen neurofibromas originate as neurinomas and become transformed to fibromas by atrophy and loss of nerve fibers. This is the view, for example, of Wallner,[99] who reported a case, which in its clinical and gross anatomic characters was a typical v. Recklinghausen's disease. He described rosette-like structures in the tissue from his case, and concluded that the neurinoma is a ripe or partly differentiated form of neurogenous tumor, and that there occur all gradations from the unripe neuroblastoma and neuroglioma to neurinoma.

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* This controversy over the participation of the sheath cells in the formation of the axis cylinder would appear to have been ended by the recent experimental work of R. G. Harrison (Neuroblast versus sheath cell in the development of peripheral nerves, Jour. Compar. Neurol., xxxvii (164), p. 123), who has shown that the sheath cells do not take part in the formation of the axon. These cells, however, are of ectodermal origin, and the neurinoma is still to be placed among the neurogenous tumors if it is derived, as was claimed by Verocay, from sheath cells.

Age Incidence of Neurinoma.—Sommer,[100] who reported two cases of neurinoma in 1922, tabulated 35 previously reported cases. Of these, only one occurred in a child, a tumor of the median nerve in a child aged six years credited to Antoni. There was one case at 17 years, and two at 18 years. Sommer, who accepted the neurogenic origin of neurinoma, believed that the tumor is quite distinct from neurofibroma, which is derived from the endo- and perineurium, and that it is the result of a developmental error which leads to the dormancy of undifferentiated embryonic nerve tissue. Erb[101] recorded three cases in 1923. Of these, one was a boy aged 17 years who had had a small subcutaneous tumor of the ulnar nerve since childhood; he later showed evidence of cranial nerve involvement. In a second case, a woman 24 years of age, the small tumor had been present in the lip since the age of 10 years. Erb added 7 cases from the literature and his own 3 to Sommer's 37 cases, making a total of 47. Of the additional seven cases reported in the literature, one occurred at six months of age, one at six years, and one at nine years. The tumor of the six months old child, credited to Harbitz, was situated in the tongue and had been present since birth. Fourteen of the 47 cases tabulated by Erb occurred in patients between the ages of 15 and 30 years. Froboese,[102] in 1922, reported a neurinoma of the base of the tongue of a girl aged 17 years, and a true neuroma composed of medullated nerve fibers, the latter forming small wart-like nodules of the tip of the tongue and of the eyelid of a boy aged 12 years. Neurinoma, like the ganglioneuroma, which it resembles in being somewhat differentiated, has been observed more frequently in young adults than in children. In many of the former, however, the tumor had been present since childhood.

Glioma.—Origin and Structure of Neuroglia.—We have discussed above tumors which contain ganglion cells (ganglioneuroma), such tumors being usually peripheral but sometimes also central in origin; those which contain embryonic formative tissue of the sympathetic system (neuroblastoma); tumors of the retina, closely related to the latter group, derived probably from embryonic neurogenous tissue of cerebral origin (neuroglioma retinæ); and tumors composed of embryonic nervous tissue of the type which enters into the formation of the peripheral nerves (neurinoma). There remains the neoplasm, relatively frequent in childhood, which is composed of the tissue which forms a prominent constituent element of the central nervous system, and which differs form most of the other tissue elements of this system in that we ascribe to it a proliferative capacity in the postnatal period which the rest of these tissues are not supposed to possess. This element, the neuroglia, is morphologically and functionally the supporting tissue of the central nervous system. Genetically, however, it is ectodermal in origin, like the rest of the essential constituents of the nervous system, and is an epiblastic hylic tissue in the terminology of Adami.[103] In its differentiated state it consists of small nuclei embedded in a ground substance, which differential staining methods prove to be finely fibrillated. Most of the nuclei are small, round, of about the size of those of small lymphocytes, and deeply stained like the latter. Other nuclei, present in smaller number, are somewhat larger, ovoid in shape, more vesicular, and apparently younger. Nuclei intermediate in character between these two are also seen. The cytoplasm may form a narrow rim about the nucleus. Sometimes the cell body is sharply defined and the cells appear to lie free in the ground substance, with no readily detectible connection with the fibrils of the latter. Or the cell body may be indistinct and may appear to be directly continuous with the fibrils.

The actual finer histologic structure of neuroglia is difficult to determine. Our modern knowledge of such structure as can be recognized has resulted from the special staining methods which have been applied and our present conception of structure varies somewhat, depending upon the method used. The original Golgi impregnation methods appeared to prove that the fibrils are the direct outgrowths of the cell bodies and that, while interlacing and anastamosing with each other, they remain connected with the cells. Weigert,[104] as the result of a method which he believed actually stained the neurologia because of the chemical differentiation of the latter, concluded that the fibrils are not directly continuous with the cell bodies, but form an intercellular fibrillated ground substance comparable to the collagenous fibrillated matrix of connective tissue. The fibrils are formed from the cells and may traverse the latter, but most of them lose their direct connection with the cell bodies. The cells are distinct entities which lie in the matrix. This conception of Weigert's was modified as the result of Held's[43] work. He agreed that most of the fibrils are not the direct processes of cell bodies, and concluded that neuroglia is a syncytium in which neuroglia fibrils differentiate and are embedded. The neurencytium is the direct derivative of the myelospongium of the early fetal medullary tube. In this syncytium cytoplasmic differentiation about some of the nuclei leads to the formation of spongioblasts, which give rise to the astrocytes of the normal adult neuroglia with their radiating fibrils. Differentiation about other nuclei leads to the formation of neurocytes, from which come the specific parenchymatous elements of the nervous system, i.e., ganglion cells and nerve fibers. Not all of the original nuclei become the nuclei of individualized cells; the neuroglia retains its syncytial character, and fibrils develop in the undivided protoplasm, in which many nuclei remain embedded without taking part in cell formation. The ependyma retains to a large degree the characteristics of the primitive neuroepithelium. Bailey[105] accepts the postnatal formation of neuroglia from ependyma. According to Schröder[106] fibrils, nuclei and distinct cells may undergo new formation independently of each other in the syncytial neuroglia in the reparative changes which occur in this tissue.

Structure of Glioma.—In view of the differences which still prevail in our conception of the structure of normal neuroglia, dependent upon the use of technical procedures which do not always give uniform results, it is not surprising that our knowledge of the finer structural details of tumors derived from neurologia is somewhat indefinite. Since the normal tissue is typically hylic in character, the gliomatous neoplasms retain the hylic features, being distinguishable with difficulty from normal neuroglia if the tumor is a slowly growing one, or having the characteristics of sarcoma if the tumor is one of rapid growth. Except for these readily detected differences in cellularity, our knowledge of the cytology of glioma is rather meager. Attention to finer cytologic details and the more general use of newer technical methods will probably reveal differences in the gliomas more important than mere variation in cellular content. Wolbach and Bailey[107] have recently made a brief preliminary report which does, in fact, indicate some quite important differences in the group of tumors usually thrown together under the heading of glioma or gliosarcoma. Based upon the study of 98 cases of brain tumor in which necropsy was done, they recognize so-called gliomas without connective tissue stroma and others with stroma. The latter include large celled tumors probably derived from ependyma, and other tumors with smaller cells which form neurofibrils, and which, therefore, they consider neuroblastomas or neurocytomas. In some of the last named tumors, typical rosettes were formed. This final recognition of the neuroblastomatous type of tumor in the central nervous system, a type of tumor whose occurrence here was to be expected in the light of our knowledge of the development of the tissues of the nervous system, is extremely important for a more exact knowledge of the histopathology and pathogenesis of brain tumors, and may have practical bearings upon the develop-

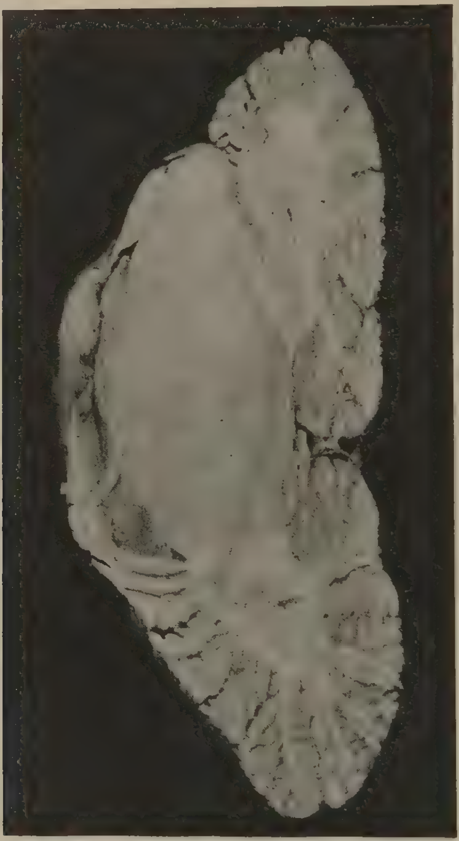

FIG. 289.—Glioma of cerebellum; female child aged 3½ years.

ment of greater refinement of clinical knowledge of these tumors. Excluding two examples of metastatic brain tumors, Wolbach and Bailey subdivided the remaining 96 tumors of their series, all being tumors of the cerebrum or cerebellum, as follows: Gliomas with stroma, 8; gliomas with cells of varying morphology (gliomas of dense type, pontine tumors), 15; gliomas with cells of varying morphology, 54; neuroblastomas, 11; mixed neurogliomas and neuroblastomas, 6; ependymal tumors of the choroid plexus, 2.

Ependymal Glioma or Ependymoma.—In the formation of fibrils, which take the neurofibroglia stain and which extend out into the surrounding neuroglia from the end of the cell away from the lumen of the ventricular and spinal canal system, the lining ependyma of this system is similar to neuroglia. In all its other features it is epithelial and retains the lepidic characteristics of the original neuroepithelium. It may give rise to tumors which exhibit a more markedly alveolar arrangement than occurs in the usual glioma. In view of the probable occurrence of neuroblastomas in the central nervous system, alveolar arrangement alone is not an adequate criterion of the ependymal origin of a given tumor. Many ependymal gliomas have been recorded, but the derivation of many of these from ependyma can not be held to be sufficiently well established. The one morphologic characteristic of the ependymal cell is the presence of minute blepharoplasts just beneath the free border of the cell; these bodies probably bear an intimate relationship to the activity of the cilia with which the free border of the embryonic ependymal cell is equipped. Using the presence of blepharoplasts as a criterion of the ependymal origin of tumors, Bailey[105] has recently (1924) reported six tumors of this type. He accepts only five of the tumors previously recorded as ependymal glioma, the latter including three tumors reported by Mallory,[108] of which one was a tumor of the fourth ventricle in a boy aged 17 years, symptoms of brain tumor having been present for two years. Of Bailey's six ependymomas, two occurred in children, both boys, one aged 7 years and the other 10 years. Both were tumors of the fourth ventricle. These six ependymal gliomas occured in Cushing's collection of "practically 900 cases" of verified brain tumor.

Incidence of Glioma in Childhood.—In Steffen's[75] compilation (Table 2), tumors of the brain and meninges ranked third in frequency among the tumors of infancy and childhood and constituted 10.52 per cent. of the tumors collected by him. In the census statistics for 1914, the relative incidence was not so high, tumors of the brain forming 1.69 per cent. of the tumors of children in this series (Table 3). Since in each tabulation these tumors were probably all gliomas, the relative importance of this tumor in childhood is apparent. Although glioma of the brain must be considered one of the most important type of tumors of children, it does not appear to be as frequent in the latter as in adults. Wollstein and Bartlett,[109] who analyzed the records of 4563 necropsies done at the Babies Hospital of New York, found nine tumors of the brain in this series. From this number they determined an incidence of 0.2 per cent., as compared with 1.0 per cent. for adults.

Origin of Glioma.—Because of the proliferative capacity of normal neuroglia, the occurrence of glioma in adult life makes possible the origin of the tumor from previously normal neuroglia. In children the tumor may be present at birth, being thus another example of congenital tumor. Other facts also point to an antenatal origin of the neoplasm when it occurs in childhood, and implicate again the phenomenon of misplacement or maldevelopment as an important factor in the origin of this as of the other tumors of childhood. Perhaps those gliomas which do not manifest themselves until later in life also arise from areas of undifferentiated neuroglia, which, because of their separation from normal relationships, have lain dormant until some unknown factor initiated progressive growth. The multiple areas of tuberous sclerosis of the brain, so frequently associated with congenital rhabdomyoma of the heart, appear to be slumbering, undeveloped neuroglia tissue, and support the possibility of the dormancy or inhibition of development of the tissue. The occurrence of neuroblastomas of the brain, as reported by Wolbach and Bailey,[107] also is evidence that undifferentiated neurogenous tissue may remain dormant within the central nervous system and give rise to tumors at some later period of life.

Cystic Glioma.—The central nervous system glioma is frequently cystic. The cyst spaces may be large, when they sometimes appear to be the result of edema, liquefaction and degeneration of the tumor tissue. Or the spaces may be small and multiple, in which case they may have a cellular lining whose character offers support to the maldevelopmental origin of glioma. The spaces may be lined by one or more layers of cells of epithelial type, which some observers believe to be ectodermal in origin and to have been misplaced during fetal life. Others believe the lining to be ependyma, which may have been misplaced by evagination from the central canal. Stolpe, according to Wisbaum,[110] reported such a glioma of the left cerebral hemisphere in a girl of 14 years, and Storch[111] one of the left cerebral hemisphere in a boy aged six years. A lining of single layered cuboidal cells, like those over the choroid plexus, has been described by Bonome[112] in a glioma of the uncinate gyrus in a six year old child. Wisbaum,[110] who has recently devoted especial attention to the lining of the cysts of gliomas, tabulated 35 examples of cystic glioma reported in the literature between 1890 and 1922. In this group the lining was described as being single layered, multi-layered, ciliated, columnar cuboidal, or ependymal in type. Seven of these 35 tumors occurred in children between the third and seventeenth years of life. She concluded that the variation in the character of the lining of the cysts might be the result of the embryonic condition of the tumor tissue, which by differentiation might form cells of variable epithelial type. Podmaniczky[113] saw, in the brain of a seven day old chick embryo, a number of canals in the brain tissue lined by a layer of cells identical with the ependyma. These canals he believed to arise by misplacement and ascribed glioma to a similar disturbance of development. It is not unusual to see, embedded in the cerebral tissue immediately about the ventricles of otherwise apparently normal brains, small glandlike structures lined by ependyma, which have apparently been formed by misplacement of the ependymal lining of the ventricles. Landau[114] also was a supporter of the view that both localized and diffuse gliomas of the brain are the result of fetal misplacement of tissue.

Heterotopic Glioma.—In the occurrence of true gliomas outside the central nervous system, misplacement appears definitely to be a factor. A congenital small glioma of the root of the nose, in a boy aged 11 days at the time of removal of the tumor, was reported by Süssenguth,[115] who believed that the misplacement had occurred through the foramen cecum. Schmidt,[116] who reported a similar tumor in a boy aged 10 weeks, concluded that the tumor had originated as an encephalocele which lost its connection with the brain. Clark[117] also has reported a glioma of the bridge of the nose, in a boy aged two years, the tumor having been present since birth. In a second case of Clark's, a boy aged 10 weeks, there had been difficulty in breathing since birth, due to obstruction of the left naris by a polypoid tumor mass. A portion of this removed by the snare was found to be composed of glia fibrils and of atypical astrocytes; he considered this tumor a glioma, but his photomicrograph shows the presence of cells which are very suggestive of ganglion cells, the presence of which would place the tumor in the ganglioglioneuroma group. Clark believed that these tumors arose by misplacement of embryonic neuroglia at the time of fusion of the halves of the frontal bone. Berblinger[118] has described the most recent example of glioma of the bridge of the nose; the tumor was present at birth and was removed when the child was three months old. Peterer[119] reported a tumor present beneath the tongue, to which it was firmly attached, in a girl aged six weeks. The tumor recurred 2½ months after removal. It was composed of dense, fibrillated stroma, fairly rich in small round nuclei; Peterer believed it to be a misplacement glioma of the tongue. A glioma of the optic nerve, without retinal involvement, has been described by Benedict;[48] this occurred in a girl aged seven years. The possible relationship of such unipotent misplacements to the totipotent or multipotent misplacements which give rise to the teratomatous or mixed tumors of the cephalic pole of the embryo has already been discussed above.

Prym's[120] sacral ependymal glioma has already been referred to in the discussion of the sacral teratomas. The glial sacral tumor reported by Scheuermann,[121] and the gluteal gliomas of Virchow[122] and of Kimpton[123] were also included under the sacral mixed tumors as the least complicated of the series. With equal propriety they might be listed here as heterotopic gliomas due to misplacement of tissue from the caudal end of the spinal cord. Prym, who included Scheuermann's case, was able to find only five other reported sacral tumors which he believed to be derived from misplacements of the caudal end of the medullary tube. He did not include Mallory's[108] ependymoma of the sacral region.

One of the most striking and unusual examples of heterotopic glioma is that reported by Askanazy and referred to by Ribbert.[124] This was a case of multiple gliomatous nodules of the lungs in a child with congenital cerebral hernia but without glioma of the brain. In this case the lung tumors were believed to have arisen as the result of the transportation to the lung by the blood stream of normal, nonblastomatous, embryonic neuroglia at the time of formation of the cerebral maldevelopment.

Glioma of the Meninges.—When a malignant glioma arises from the subependymal tissue of the ventricular system it may reach the meninges and cause widespread, diffuse gliomatosis of the leptomeninges. Firor and Ford,[125] who reported such a condition in a boy aged 15 months, found three similar cases in children in the literature previous to their report (1924). In an article on sarcomatosis of the meninges, in which their case of gliomatosis was also included, Ford and Firor[126] made the statement that most of the cases of so-called diffuse sarcoma of the meninges are probably gliomas. Löwenberg,[127] who reported two cases of diffuse glioma of the meninges, in children aged 11 months and 12 years respectively, believed that diffuse meningeal glioma is rare as compared with diffuse sarcoma. These two cases were not included in Firor and Ford's tabulation.

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BENIGN TUMORS

In the preceding discussion the teratomas and mixed tumors, the rhabdomyomas, and the tumors derived from the elements of the nervous system have been considered in detail because these are the characteristic neoplasms of the early years of life. They are not limited in their occurrence to this period, but their incidence is higher than at any later period, and some, like the mixed tumor of the kidney and the neuroblastoma of the adrenal and sympathetic system, are limited almost exclusively to childhood Even when the tumors of this group do not manifest themselves until adult life or are chance necropsy findings in adult life, they are still to be considered neoplasms characteristic of the developmental period because in all of them misplacement or inhibition of development during the fetal period appears to be a fundamental factor. Whereas the tumors discussed above may be delayed in their appearance until adult life, other kinds of tumors, which are usually associated with this later period, may make their appearance during childhood. The pediatrician must, therefore, constantly bear in mind the possibility of the occurrence of any kind of tumor in his patients, but at the same time should be guided by the relatively greater frequency of certain tumors in childhood in determining the probable character of any given neoplasm. In what follows the various kinds of tumors will be considered from the standpoint of their occurrence in children.

Hylic Blastomas of Mesoblastic Origin

Fibroma.—The fibroma is a tumor composed of the type of fibrous tissue so widely distributed throughout the body, and may arise, therefore, from this tissue anywhere. It is usually firm, pale, dense, poorly vascularized, only slightly cellular, and usually sharply defined or encapsulated. Subcutaneous fibromas (Fig. 290), and keloids developing in scars, may be poorly defined and not encapsulated. Sometimes the tumor is softer, more cellular, poor in intercellular ground substance, to such a degree that it may be difficult to decide whether the neoplasm is to be considered a benign fibroma or a moderately malignant fibrosarcoma. Some of the fibromas of children may be richly vascularized.

As examples of fibromas of children unusual because of their location, Merkel[1] mentions one of the frenum of the prepuce of the penis and one of the vulva. Sublingual fibroma, usually in the form of a small polypoid mass attached to the frenum of the tongue, is said to be frequent in Italy and France; Callari and Phillipson[2] reported four German cases. Debenetti[3] described a fibroma of the gubernaculum hunteri in a four year old boy. The tumor, which measured 4.5 by 2.5 cm., was encapsulated and was loosely attached to the testis and epididymis.

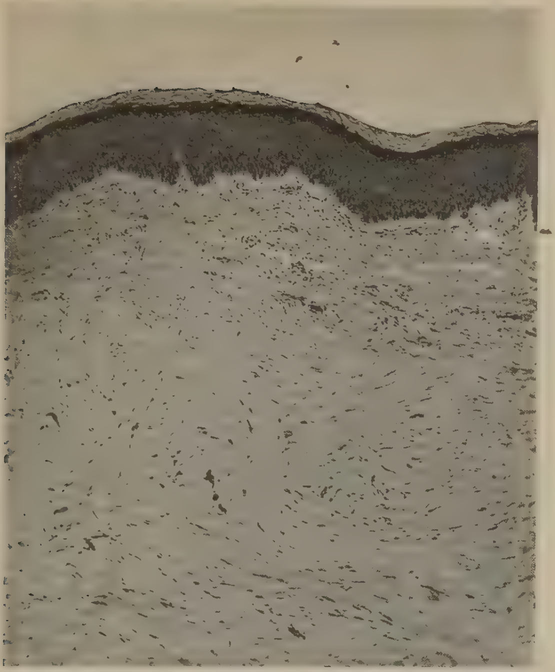

FIG. 290.—Fibroma of skin; boy aged 8 years. ×80.

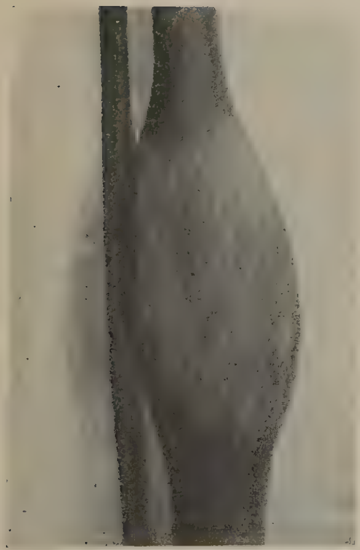

FIG. 291.—Roentgenogram of central fibroma of tibia. (Beck.[5])

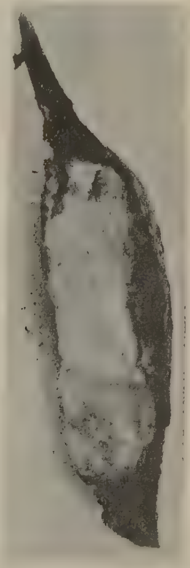

FIG. 292.—Central fibroma of tibia. (Beck.[5])

The tissue was soft and cellular, in part mucoid and embryonic in character. It contained a few giant cells. Debenetti derived the tumor from embryonic connective tissue at the insertion of the gubernaculum. The presence of giant cells raises a question as to whether this neoplasm may not really have been a rhabdomyoma, the possible origin of which from the gubernaculum has been discussed above. Deming's[4] tabulation of 65 primary tumors of the urinary bladder in the first decade of life includes five fibromas.

An unusual central fibroma of the tibia was reported by Beck[5] in a girl aged 19 years. It had been present since the age of six years and had caused a smooth, fusiform enlargement of the upper part of the tibia (Fig. 291). The periosteum was normal. The tumor was sharply defined, had completely replaced the marrow, and had caused thinning of the covering bone (Fig. 292). Beck believed that the tumor arose from the connective tissue of the marrow, but considered also the possibility that the so-called "giant cell sarcoma" of bone may be transformed into such a fibroma. He could find only one similar case in the literature, that of Frangenheim in a girl of 9 years. In this case the tumor was a recurrence of a mass removed from the tibia when the child was four years old, the histologic diagnosis at that time being osteoid fibrosarcoma. At the second operation the marrow cavity was found occupied by masses of pale, dense tissue; Frangenheim's diagnosis was ostitis fibrosa. Small, single or multiple fibromas of the renal medulla are not infrequent. They are of no clinical significance, but are of interest as maldevelopments of the type termed hamartoma by Albrecht. Some of them may be composed wholly of fibrous tissue; others may contain a few compressed, atrophic medullary tubules (Fig. 293). Karrenstein's[6] compilation of 39 non-myxomatous tumors of the heart included a fibroma of the ventricular septum of a child aged three months and one of the anterior wall of the right auricle in a child of 10 months.

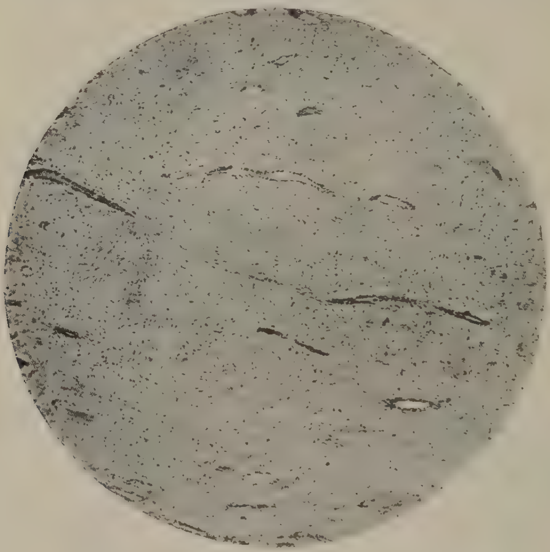
FIG. 293.—Fibroma of renal medulla. ×60.

Recurrent Fibroma of the Nasopharynx.—One form of fibroma deserves special mention because it is limited in its occurrence to the adolescent period of life. This tumor, the recurrent fibroma of the nasopharynx, was known to Hippocrates, who described a method for its operative removal. It arises in the vault of the pharynx, or in the posterior nasal fossæ according to Canuyt,[7] and is believed to come from the fibrocartilage of the basilar process of the occipital bone, of the upper cervical vertebræ, or of the internal lamina of the pterygoid process of the sphenoid bone. Although supposed to arise from fibrocartilage, it contains no catilage and is composed of dense fibrous tissue and is usually richly supplied with blood-vessels in its peripheral zone. Adami[8] derives the tumor from the submucous connective tissue of the nasopharynx and places it among the blastomatoid conditions. It may be pedunculated and may become attached to the soft parts with which it comes in contact.

The nasopharyngeal fibroma has pecularities other than its occurrence during the second decade of life. Although it is said to occur almost exclusively in males, Alonso[9] in 1924 was able to find 13 recorded cases in females. It usually undergoes spontaneous regression when the bearer reaches the age of 20 to 25 years. In spite of the fact that the tumor is histologically benign, that it does not metastasize, and that its spontaneous regression may take place, the prognosis is grave. It grows by extension into the nasal fossæ and sinuses. Trautmann[10] has reported one in a boy aged 15 years which also grew downward into the larynx. Its growth may cause atrophy of the base of the skull, permitting the tumor to reach the orbit; or infection of the meninges may occur by way of the nasopharynx, resulting in death from meningitis. Not only does the tumor have these untoward effects through its mechanical action, but it also usually recurs after removal. The recurrence may be histologically just as benign as the original tumor. Occasionally the original tumor is so cellular as to suggest fibrosarcoma, but cellularity is not a prerequisite for recurrence. The proneness to recurrence is attributed by Adami[8] to a blastomatous or blastomatoid tendency present diffusely in the stroma of the nasopharyngeal tissues in certain individuals. Bleeding is the most important clinical symptom.

Because of the broad attachment which the tumor may have, surgical removal is hazardous and the immediate operative mortality is high. The surgical risk is an important factor because of the tendency of the neoplasm to recur. Crowe and Baylor[11] advised conservative treatment. In a series of 49 benign and malignant growths of the nasopharynx subjected by them to radium treatment, there were four examples of nasopharyngeal fibroma. These were in males aged respectively 15, 16, 18 and 20 years. Two of the four were considered cured by radium and two were reported as improving. New and Figi[12] reported a study of 32 cases seen at the Mayo Clinic in the years 1910 to 1923 inclusive. In this group the age varied from 10 to 31 years, 29 being less than 25 years old; the activity of the tumor seemed to be directly related to the age of the patient. Twenty-eight were males and four were females. Twenty-three had been subjected to previous operations, most of them several times. In 10 cases the tumor was confined to the nasopharynx; in 13 it had extended into both nostrils; the antrum was invaded in 2 cases, and the palate in 3. The tumor originated on the right side in 18 cases, on the left side in 9, and in the median line in 3. New and Figi agree with Crowe and Baylor that radium is the treatment of choice.

Recurrent Fibrous Nasal Polyps of Children.—A tumor similar in many respects to the nasopharyngeal fibroma is the recurring nasal polyp recently described by Canuyt and Terracol.[13] According to these authors the usual myxomatous form of nasal polyp is rare in children under 14 years of age. The nasal polyps below this age are constant in type. They are bilateral, they are usually situated in the middle fossæ, and they recur rapidly after removal. They may reach a large size and they may be multiple. Histologically they are poorly vascularized, and they are dense and fibrous. They may cause an abundant mucous discharge and complete nasal obstruction with loss of the sense of smell. They are unlike the nasal polyps of adults, which usually deform only the cartilage and soft parts, in that they cause pressure necrosis of the nasal and ethmoid bones. In their destruction of bone, in their histology, and in their tendency to recurrence they are much like the nasopharyngeal fibromas; unlike the latter, they appear to occur with about equal frequency in the two sexes. Canuyt and Terracol believed that congenital syphilis might be a factor in their formation.

Hypertrophy of the Gums.—A blastomatoid condition, considered by some to be a fibroma, is diffuse, primary hypertrophy of the gums, which may be congenital or develop early in life. Both jaws are usually involved. Simple removal of the redundant tissue is generally followed by recurrence. Ruggles[14] has described two cases in a family in which there had been ten cases, all apparently transmitted through the female members of the line.

Neurofibroma.—v. Recklinghausen[15] showed that the tumor which develops along the course of the nerve trunks is derived from the connective tissue endo- and perineurium, and is, therefore, a fibroma and not a neuroma. It is composed usually of dense fibrous tissue arranged in interlacing bundles, with which the original nerve fibers are intermingled. The latter may show degenerative changes and may finally disappear completely. At times the tissue is more cellular, and sarcomatous transformation is not rare. The fibroma of nerves, or neurofibroma, may occur as an isolated, single tumor nodule along the course of any nerve. Kriege[16] described such a solitary neurofibroma of the cheek in a girl aged five years, the tumor having arisen in a terminal subcutaneous nerve. Fourteen solitary fibromas of nerves seen by Harbitz[17] occurred in adults between the ages of 20 and 40 years. A tumor of the optic nerve, described by some as fibroma and by others as fibrosarcoma, is more frequent in children than in adults; four of five optic nerve tumors seen by Harbitz occurred in children aged respectively 5, 8, 11 and 13 years. The tumors were more cellular than the usual fibroma, but they were well circumscribed, encapsulated and did not invade. Harbitz believed that the tumors reported as fibroma or sarcoma of the optic nerve are gliomas and should be classed with the retinal gliomas. The propriety of considering the latter true gliomas has already been discussed. The optic nerve tumors of Harbitz are apparently the same neoplasm described by Ewing[18] as neuromyxomas or myxogliomas of the optic nerve. They are benign, and if recognized early enough may be removed without damage to the optic nerve.

Neurofibromatosis.—More frequent and more important are the examples of multiple tumors along the course of many of the nerves, the condition known as v. Recklinghausen's disease or neurofibromatosis. The tumors, which may begin to make their appearance in the early years of life, increase in size and in number, until tens and hundreds of nodules of varying size may be counted. The growth of the individual nodules is slow, but tends to become more rapid after puberty. Although neurofibromatosis may involve the deep as well as the subcutaneous nerves, it is the involvement of the latter which produces or is associated with striking changes in the skin that make v. Recklinghausen's disease a most unusual pathologic and clinical entity. Localized thickening or elephantiasis of the skin, known also as pachydermatocele, due to hyperplasia of the subcutaneous connective tissue, may lead to the formation of deforming pendulous masses. In the latter the tissue may become edematous and degenerated, a condition to which the term dermatolysis has been applied. The tissue hyperplasia may be diffuse and may cause elephantiasis of an entire limb.

Cleuet and Ingelrans,[19] in 1923, reported a case of congenital elephantiasis of the scrotum due to neurofibromatosis; at nine months of age the enlarged scrotum reached to the calf of the leg. Neurofibromatosis of the nerves of the mesentery has been associated with marked thickening of the intestine. In Baltisberger's[20] case of mesenteric neurofibromatosis, fibrous hyperplasia of the mucosa was part of the involvement of the submucous Meissner's plexus; the intermuscular Auerbach plexus itself was normal, but the nerve branches leading to it from the neurofibroma of the mesentery were thickened. Within a single year (1924) the writer has seen two examples of enlargement of the appendix due to thickening of the submucosa by neurofibromatosis. Another unusual localization of neurofibromatosis is the tongue, resulting in unilateral or symmetrical macroglossia. Such cases have been reported by Abbott and Shattock[21] in a four year old girl (Fig. 294), in whom the enlargement had been present since the age of two months; by Delfino,[22] in a three year old child, whose tongue had been involved since birth; and by Hayashi,[23] in a boy aged three years. In Abbott and Shattock's case and in the case of a 10 year old boy reported by Thomson and referred to by Abbott and Shattock, the lesion of the tongue was associated with neurofibroma of the side of the face and head.

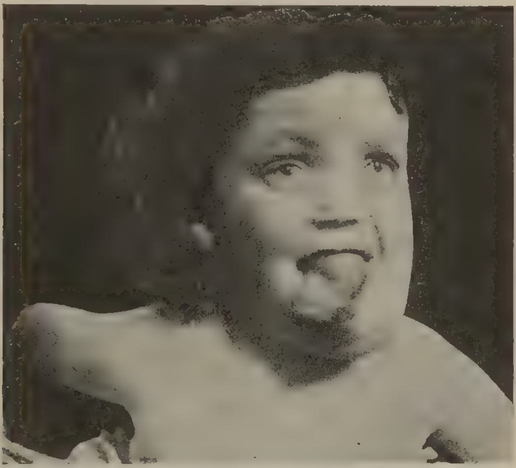

FIG. 294.—Neurofibroma of tongue in a girl aged 4 years. (Abbott and Shattock.[21])

The skin, in addition to elephantiasis, may show pigmentation, hypertrichosis, pigmented or angiomatous nevi, wart-like excresences, and small, soft tumor nodules (molluscum fibrosum). The thickening of the skin and the formation of discrete nodules are the result of hyperplasia of connective tissue, which appears to take its origin from the hyperplastic tissue of the nerves; sometimes, however, the relationship of the nodules to nerves can not be established. The bones beneath the involved tissue may be enlarged and hyperplastic. The bone changes associated with v. Recklinghausen's disease have recently been discussed by Brooks and Lehman,[24] Weiss,[25] Stahnke,[26] and Gould.[27] When the vertrebral column is involved there may be marked scoliotic or kyphotic deformity. The osseous changes, like those of the skin, are believed to be the result of diffuse hyperplasia of the periosteum when the nerves of the latter are involved. Resorption and new formation of bone are associated with the thickening of the periosteum. Sometimes the bones may show absorptive changes, without periosteal involvement, due to pressure of overlying tumor nodules of the nerves. In the seven cases of Brooks and Lehman's[24] series with bone changes, the ages of the patients at the time of observation were respectively 4½, 9, 11, 12, 19, 22, and 41 years. Neurofibromatosis is frequently associated with psychic defects, even in cases which are free of detectable involvement of the brain or of the cranial nerves.

v. Recklinghausen's disease is characterized by a strong hereditary or familial element. Hoekstra,[28] who saw neurofibromatosis in father and son with a change to malignancy in each, investigated the questions of heredity and malignancy in the reported cases. He was able to find 63 reported families in which neurofibromatosis had occurred and in which there appeared to be an hereditary factor. In 12 of these families there was not only neurofibromatosis in more than one generation but also malignant transformation in one or more generations. The hereditary element does not always manifest itself by involvement of the nerves; certain members of the family may show hypertrichosis, skin pigmentation, or psychic changes without tumors of the nerves. Acuña and Bazan,[29] who recently reported eight cases of congenital v. Recklinghausen's disease, made the statement that the disease is usually of an incomplete, abortive type in children, and may therefore be overlooked.

There has been much discussion as to whether the axis cylinders themselves take an active part in the process. The consensus of opinion is that there is no actual new formation of nerve fibers, although Kriege,[16] Wegelin[30] and others believed that there is participitation on the part of the axis cylinders in that the latter must increase in length to account for the tortuous course of the nerve fibers. Neurofibromatosis appears to be more than a condition of simple tumor-like hyperplasia of the connective tissue of nerves. It is a system disease whose basis is an embryonic maldevelopment, which manifests itself not only in the formation of the characteristic nerve tumors but also in the striking associated changes.

Racemose Neurofibroma.—Certain cases, which in other respects belong to the v. Recklinghausen's disease group, differ from the usual type with its multiple, more or less separate tumors of the nerves widely distributed in the body, in that the tumor formation is limited often to a single area, which is the seat of a nodular mass of variable size. The mass is composed of closely placed and united nodules, which closer examination shows to be connected with nerves. The skin over the tumor may be the seat of elephantiasis, hypertrichosis or pigmentation, as occurs in the more usual forms of neurofibromatosis. For the more localized form of tumor, with its nodular, worm-like mass of thickened nerves, Bruns[31] proposed the name *Ranken-Neurom.* By others the term plexiform neuroma has been used, and the two terms have become somewhat interchangeable.

Strauss,[32] in a paper published in 1906, reported such a localized multiple neuroma of the lumbar region (Fig. 295) in a boy aged 12 years. The tumor had made its appearance as a small nodule at the age of two years. It grew slowly until it reached a size 9 cm. in diameter, and was closely attached to the underlying fascia and to the overlying skin, which was pigmented and covered with hair in an area measuring 32 by 14 cm. From the nodular tumor mass a pedicle could be followed through a spina bifida occulta to the dura. Strauss made this case the basis of a thorough study of the so-called plexiform neuromas, and concluded that these may be subdivided into two groups which show some rather striking differences. For the one group he proposed the name *Rankenneurom*, which may be translated racemose or circoid neurofibroma, and for the other group the name plexiform neurofibroma. He retained the older designations, but attempted to characterize and define each more sharply than had previously been done. Wegelin[30] accepted the distinction made by Strauss, but Baltisberger[20] did not believe that such a sharp differentiation was possible.

The racemose neurofibroma consists of firmly united masses of nodules, lying upon and beside each other, which can not readily be unravelled into a definite plexus or network. There is usually a pedicle which can not be identified with any particular nerve trunk. The tumor is as a rule limited in its occurrence to the head and trunk, being situated about the orbit or in the eyelid, in the region of the ear, in the posterior cervical or occipital region, or in the lumbo-sacral region. These are the regions where meningoceles, encephaloceles, or myeloceles are most prone to occur as the result of developmental bony defects. The racemose neurofibroma of these situations is also frequently associated with such bony defects, which many writers have believed to be secondary to the tumor and due to pressure atrophy. Strauss, however, believed that the bone defect is a fundamental and essential part of the neurofibromatous process, the pedicle of the tumor making its way through the defect to the membranes or tissues of the central nervous system. Wegelin,[30] who reported two cases of racemose neurofibroma of the occipital and temporal regions in two boys aged respectively 13 and 14 years, agreed that the bone defects, when present, were the result of maldevelopment, but he did not concede that the defect was an essential part of the neurofibromatous process, because the tumor or its pedicle need not come through the opening in the bone. Hanke,[33] who reported two cases of racemose neurofibroma of the eyelid in girls aged respectively 13 and 18 years, the tumor in each case having been present since childhood; and Delfosse,[34] who reported a similar tumor of the eyelid, present since birth, in a girl aged three years, called attention to the relative frequency of occurrence of this form of tumor in the eyelid, a fact confirmed by others

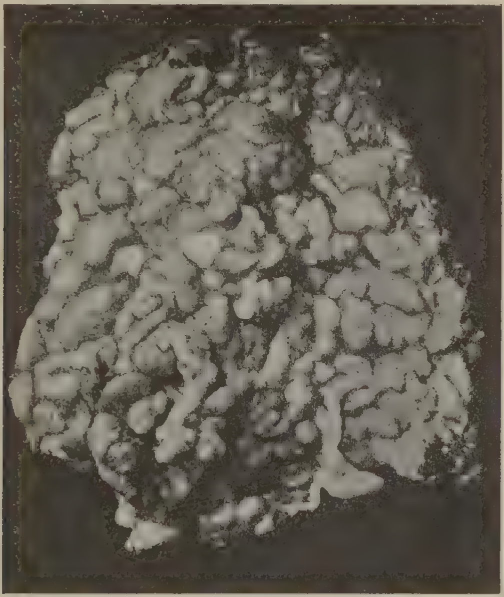

FIG. 295.—Racemose neurofibroma of lumbar region in a boy aged 12 years. (Strauss.[32])

who have followed them. The racemose neurofibroma usually grows slowly, and is painless except on pressure. It may show periods of greater growth at puberty, menstruation, pregnancy or lactation. It usually does not recur after removal. Strauss claimed that malignancy had not occurred in any tumor of this kind described up to the time of his report. In one of Wegelin's tumors one nodule was cellular and was believed to be undergoing early sarcomatous change, although it was still well encapsulated.

Plexiform Neurofibroma.—The plexiform neurofibroma is situated almost exclusively upon the extremities and arises from one or more branches of the brachial plexus or of the sciatic nerve. In its general gross appearance it is much like the racemose neurofibroma, but upon careful dissection can be unravelled into a plexus or network (Fig. 296), into which the normal nerve can usually be traced at the central end of the tumor; at the distal portion of the tumor, normal nerve branches can be seen to leave the mass. The tumor may be associated with the same changes in the overlying skin as occur in racemose and multiple neurofibromatosis. The plexiform variety usually comes to observation at a somewhat later age than racemose neurofibroma; it grows more rapidly; it is often spontaneously painful, the pain being lancinating in character; and malignant transformation is not infrequent. It may recur after removal. Psychic changes occur about as often in the plexiform as in the multiple form of neurofibromatosis, but are less frequently associated with the racemose form of tumor.

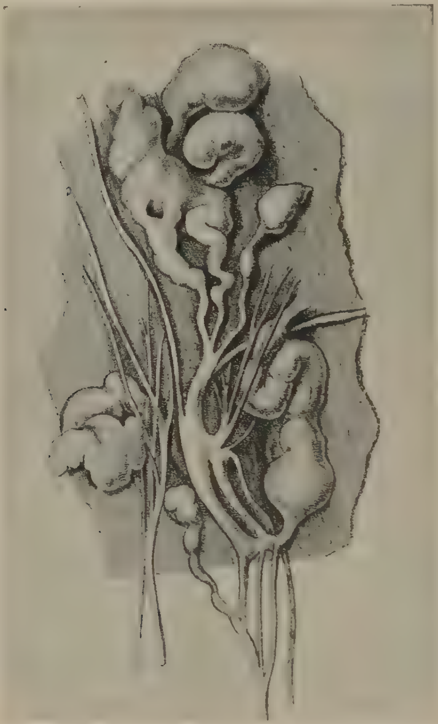

FIG. 296.—Plexiform neurofibroma. (Bruns.[31])

Relative Frequency of Racemose and Plexiform Neurofibroma.—Strauss[32] collected 112 cases reported previous to 1906. Of these, he classed eighty as racemose and 32 as plexiform. He excluded 16 of the first group and 4 of the second as uncertain, because of incomplete data. In the remaining 92 cases the sex was given for 88 and was distributed as follows: Racemose neurofibroma, 37 males and 26 females; plexiform neurofibroma, 16 males and 9 females. This slightly greater preponderance of males over females holds also for multiple neurofibromatosis. In some tabulations of the latter the male cases constitute 65 per cent. of the total, although in small series reported by individual observers females may outnumber males, as in Harbitz'[17] group of 14 cases of multiple neurofibromatosis, of which 10 were females and 4 males. Either typical racemose or plexiform neurofibroma may be associated with multiple isolated fibromas of the nerves. When a localized area of racemose or plexiform neurofibromatosis is present, the tumor may be surgically removed, usually without evidence of motor or sensory disturbance in the distribution of the nerve. Because of the accession of growth which may occur at puberty, Strauss recommended that removal should be done before this period. The prognosis after removal is good in the racemose variety, but should be more guarded in plexiform neurofibromatosis, because of the greater tendency to recurrence and malignancy in the recurrent nodules.

Myxoma.—The term myxoma should be reserved for the tumor which is composed of stellate, branching cells and a soft, semifluid, homogeneous matrix which gives the reaction for mucin. The normal homologue of this tissue is the Wharton's jelly of the umbilical cord. True myxomas are rare; usually this name is applied to fibromas whose tissue is edematous and more or less degenerated. Although the pure true myxoma is an infrequent neoplasm, areas of such embryonic tissue are not unusual in other tumors, especially in some of the mixed tumors and in those containing embryonic cartilage.

A myxomatous tumor of a kind of which there are quite a number in the literature is the myxoma of the heart, occurring most frequently in the auricle, but also upon the valves and the ventricular endocardium. Karrenstein,[6] who reported a myxoma of the left ventricle of an adult, collected 38 examples from the literature previous to 1908. Six of these were in children; four were situated in the left auricle, one on the wall of the left ventricle, and one on the wall of the right ventricle, the last consisting of multiple small nodules. Sudden death occurred in two of the children; the others had shown symptoms of cardiac disease previous to death. Husten,[35] who gave a complete summary of the cardiac myxomas to 1923, believed that most of them are organized thrombi and not true tumors. Karrenstein considered the presence of elastic tissue proof of the neoplastic character of the lesion and suggested the name fibroelastomyxoma.

Leitao[36] reported a case of bilateral myxoma of the feet in a boy aged 11 months; a mass the size of a hen's egg, present on the dorsum of each foot at birth, increased slowly in size. He found recorded in the literature a myxoma of the foot which later involved the subcutaneous tissue to the knee; one of the tibia; one of the omentum; and one of the thymus. Dabney[37] reported a myxoma of the pharynx in a girl aged 12 years.

Lipoma.—The lipoma, composed of adipose tissue which differs from normal only in the smaller size of its fat cells, occurs usually in those situations where adipose tissue is normally found, although in a few instances the tumor has been situated in a region where adipose tissue does not normally occur.

The most interesting of the heterotopic lipomas are those which have been described in the central nervous system or its membranes. Some of these, examples of which have been reported by Zuckermann[38] and by v. Sury,[39] contained bone or other tissues and belong more properly among the mixed tumors. At other times they are associated with spina bifida and again appear to be the result of maldevelopment. The fatty tail-like appendages also apparently are malformations rather than blastomas. Zuckermann[38] mentioned a pea-sized lipoma of the region of the corpora quadrigemina in a boy aged 10 years, reported by Spieler, and a lipoma of the corpus callosum in a 15 year old girl, reported by Bartel. Wolbach and Millet[40] described a case of diffuse subdural lipomatosis of the spinal cord in a boy aged 10 months. The entire pia of the cord from the medulla to the terminal filiament was diffusely and symmetrically thickened by the presence of adipose tissue. They were able to find one previously reported similar case in a child, a girl aged five years.

Nogueras[41] successfully enucleated a lipoma of the fibula weighing 785 gms. in a boy aged nine years. A lipoma of the scalp, a situation in which lipoma is rare at any age, has been reported by Cutler[42] in a boy aged two years and four months; the tumor had made its appearance at the age of four months and had increased steadily in size (Fig. 297). Melchior[43] had reported a case in 1917, in which the tumor of the occipital region appeared at the age of 11 weeks and increased rapidly in size, becoming as large as a man's fist. He found ten previously reported cases, all of which, like his own, were deeply situated, that is, beneath the aponeurosis and directly upon the bone. Tull and Alam[44] have reported a lipoma weighing 51 lb., removed from the breast of a girl aged 11 years. Bilateral symmetrical hypertrophy of the breasts in young girls appears to be the result of diffuse hyperplasia of adipose tissue rather than of tumor formation; in a case credited to Königsberger by Merkel,[1] each breast, in a girl aged 12 years, weighed 35 lb. Somewhat similar diffuse hyperplasias of adipose tissue have been noted by Baumgärtner (cited by Merkel[1]) in the hand of a child, and by MacAusland and Wood[45] in a case in which both feet were involved at birth. In each of these cases a limited local operation was followed by further increase in adipose tissue which rendered more extensive operation necessary. Variot and Monod[46] reported symmetrical bilateral lipomas of the soles of the feet in a child aged 1½ years; similar symmetrical tumors had made their appearance on the soles of the mother's feet during the seventh month of pregnancy. In the intestinal tract submucous lipomas may become pedunculated and may cause obstruction, either by their size or through invagination of the intestine. A subpleural lipoma reported in

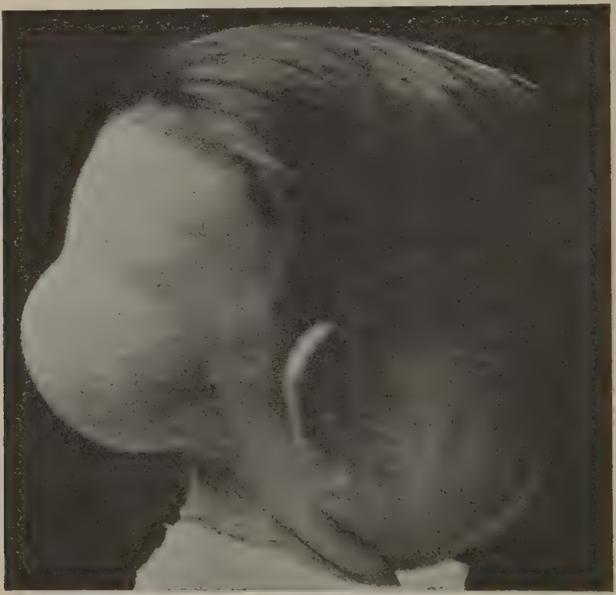

FIG. 297.—Lipoma of scalp; boy aged 2⅓ years. (Cutler.[42])

1923 by Beyers[47] occurred in a boy aged 22 months and had been present since the age of 10 months, increasing steadily in size from the time of its first appearance. The subcutaneous mass was pedunculated, the pedicle penetrating the sixth costal interspace and being continuous with a second, smaller lipomatous mass situated subpleurally in the anterior mediastinum.

The sucking pad, or the buccinator adipose body of Bichat, may give rise to lipoma of the cheek. Ransohoff,[48] in 1917, reported two cases of congenital lipoma of the pad, one in a girl aged six months, the other in a girl five years old (Fig. 298). In the latter case an attempt at removal had been made when the child was one year of age. Cameron,[49] who reported an additional case in a boy aged 14 years in 1921, collected and summarized the previously reported cases, of which he was able to find 15, in nine of which the tumor was definitely stated to have arisen from the pad. In his own case the mass had been present ever since the patient could remember, but had become externally visible only two years before coming under observation. The only patients who came under observation during the period of childhood were the two of Ransohoff and the one of Cameron, and in these the tumor may be considered congenital. In an additional case, previously reported by v. Bruns, although not seen until 19 years of age, the mass had been present since birth. In the remaining cases the age of onset was put at 10 to 62 years. Of the total sixteen cases, seven were males, seven females, and in two the sex was not stated. The right side was involved ten times, the left three, and in three the side was not stated. The tumors varied in size from that of a chestnut to that of a fist. Ransohoff,[48] who reviewed the reported cases of lipoma in children, mentioned two of the calf and one of the dorsum of the foot.

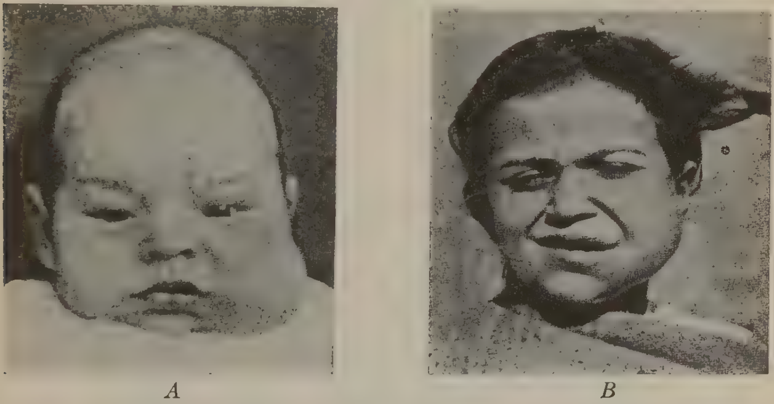

FIG. 298.—Congenital lipoma of sucking pad. A, girl aged 6 months; B, girl aged 5 years. (Ransohoff.[48])

An unusual form of congenital lipoma is the bilateral lipoma of the round ligaments, described by Ducuing[50] in a girl aged five years, believed by the author to be the only example of this condition reported. It was first noted at birth as a small tumor of the left inguinal region, and at three months of age a similar tumor appeared in the opposite inguinal region; the diagnosis at this time was bilateral congenital inguinal hernia. Progressive increase in size led to a later diagnosis of bilateral congenital inguinal eventration, in spite of the fact that there had never been any gastro-intestinal symptoms. When the child came under Ducuing's observation the lower abdominal region was enlarged by two symmetrical masses which extended downward and involved both labia majora (Fig. 299). At operation there were found two distinct encapsulated fatty tumors, which could be easily separated from the labial tissues. There was no hernial sac; the external opening of each inguinal canal was small, and each round ligament could be followed from its tumor mass into the canal. The left tumor weighed 143 gm., the right 92 gm. The tumors were believed to have arisen from the subperitoneal fat or from Imlach's plug attached to the external end of the round ligament.

Fatty tumors may contain fibrous tissue in amounts greater than is usual for normal adipose tissue, or more rarely they may be unusually vascular. Kay[51] has reported a cystic fibrolipoma of the pelvis in a girl four years old, which was unusual because of the sudden onset of the symptoms which it caused. The latter were pain and inability to urinate. The tumor, which measured 10 by 5 cm., was attached to the bladder at one side and to the ilium at the other. Woodman[52] has recorded a fibrolipoma of the tongue in a young woman aged 20 years. It had been present for a number of years, during which time she complained of a "lump in the throat." The lump proved to be a pedunculated tumor the size of a duck's egg, which was attached at the dorsum of the base of the tongue and overhung the epiglottis. A tumor reported by Milward[53] was an angiolipoma of the parotid in a child of 10 months. The tumor grew rapidly during the final two months before removal; the parotid and the neoplasm were so intimately united that both had to be removed together.

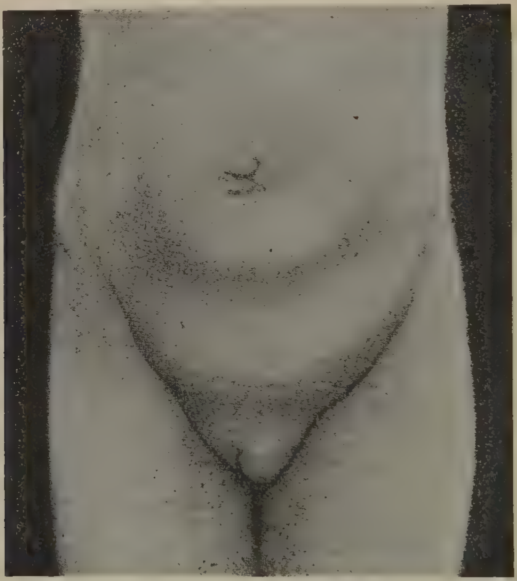

Fig. 299.—Bilateral congenital lipoma of round ligaments; girl aged 5 years. (Ducuing.[50])

Xanthoma.—That the various conditions to which the term xanthoma has been applied are all true tumors appears doubtful. The xanthoma, so-called, is characterized by the presence of large ovoid cells filled with small lipoid droplets. The latter may coalesce to form larger masses and the surrounding cell membranes may disappear. Kirch[54] is probably correct in looking upon the xanthoma cells as the cells of fibromatous or sarcomatous tumors or of inflammatory or normal tissues which have become filled with lipoid as the result of an infiltrative or degenerative process. In some cases, at least, this condition appears to be the result of disturbed cholesterol metabolism. The most interesting form of xanthoma in children is that known as xanthoma tuberosum multiplex, a condition recently reviewed by Knowles and Fisher.[55] In their case, a boy aged 10 years, the yellowish tumor masses were present in the gluteal region (Fig. 300), and over the elbows, ankles and heels.

Leiomyoma.—Tumors composed of smooth muscle, usually intermingled with fibrous tissue, while very frequent in adults, are rare in children. In the latter they have usually been situated in the skin, are frequently multiple, and come from the smooth muscle of blood-vessels or from the arrectores pilorum. In a case reported by Hess,[56] a girl aged 19 years, multiple small nodules in the skin of the nose first made their appearance at the age of three years. They increased only slightly in size and were painless. Hess believed that they were derived from the blood vessels. He mentioned also a case of Hardaway, in which multiple skin myomas of the trunk and extremities had been present since the age of three or four years. Lieber,[57] who reported three cases of multiple leiomyoma of the skin in adults and one of solitary leiomyoma in a child, concluded that the multiple tumors arise from the arrectores pilorum, the solitary ones from the blood-vessels. His solitary tumor occurred in a child aged four weeks and had been present since birth; it was situated at the outer side of the knee. He collected 77 previously reported cases of leiomyoma of the skin. Most of these were in individuals who had reached adult age when they came under observation, but 13 were children or the tumors were known to have been present since childhood. Deming's[4] tabulation of bladder tumors in children included one myoma.

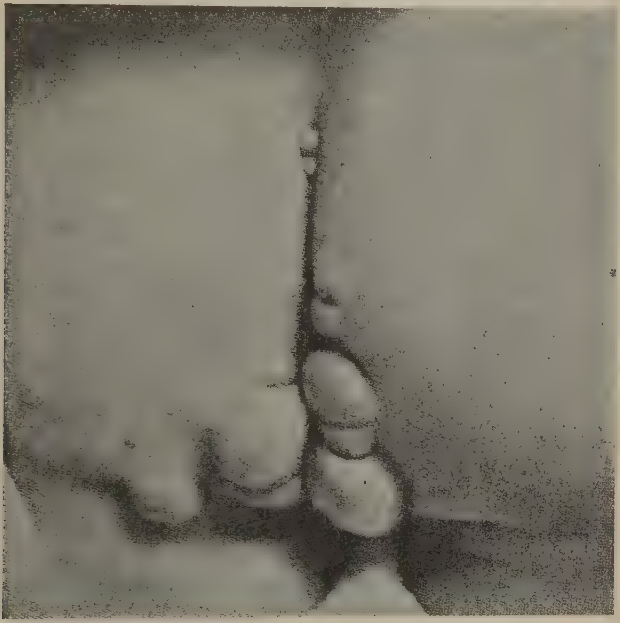

FIG. 300.—Xanthoma tuberosum of perineal region; boy aged 10 years. (Knowles and Fisher.[55])

The rhabdomyomas have already been considered above

Chondroma. Ecchondrosis.—An excessive formation of cartilage may make itself evident in childhood in those situations where cartilage normally exists, that is, at the growing ends of the long bones and at the costo-cartilaginous junctions. The process may result in the formation of multiple tumor-like enlargements, often somewhat irregular in outline, closely attached to the skeleton. When situated near the joints they may interfere with the movement of the latter. The cartilage is usually well differentiated and similar in structure to that of the epiphyses from which it arises. It is subject to degenerative changes, especially of a mucoid character, which may lead to cyst formation in the cartilaginous masses. Calcification may occur, and there may be true bone formation. A similar condition of hyperplasia or ecchondrosis of pre-existing cartilage has been seen in the lung, where multiple small cartilaginous nodules may be attached to the bronchi.

Solitary Chondroma of Long Bones.—As the result, apparently, of misplacement of cartilage into the shaft of a long bone from the epiphysis, there may arise solitary chondromas of the long bones. These lead usually to expansive enlargement of the bone, most often at the upper end of the femur, less frequently at the upper end of the humerus. The cortical bone is atrophied and thinned or remains undeveloped over the cartilaginous mass. The condition is seen in children and young adults. Degeneration of the cartilage may lead to transformation of the chondroma into a bone cyst, and in time the cartilage may disappear so completely that it is impossible to determine the origin of the cyst. Röpke[58] tabulated 33 reported cases of solitary cyst of the long bones. All of these except one were in children or in young adults below the age of 22 years. In 14 of the total number the cyst was believed to have arisen by degeneration of a cartilaginous tumor. Of this group of cystic chondromas, two were situated at the upper end of the humerus, the rest at the upper end of the femur.

Misplacement Chondromas.—Cartilaginous masses may be found in places where this tissue does not normally occur. Such masses, which are the result of misplacement, may exhibit slow but progressive growth and lead to the formation of small, tumor-like nodules. They are seen most often in the neck, where they may be symmetrical on the two sides, as described by Buttersack,[59] or present on only one side, as in Bidder's[60] case. They arise as misplacements or remnants of the branchial cartilages, an origin ascribed by several observers to the cartilage which may be present in mixed tumors of the salivary glands or in the capsule of the tonsil. Cartilage is a frequent constituent of teratomas of the thyroid and neck, here originating also from branchial misplacements. In the region of the neck we have again, therefore, examples of tissue heterotopia, which is the result of embryonic displacement, the complexity of the heterotopic tissue depending upon the unipotent, multipotent or totipotent qualities of the misplaced anlage.

The chondroma furnishes one of the examples of the rare phenomenon of metastasis of well differentiated, apparently benign tumor tissue. This process has been explained by the proneness of chondroma to mucoid degeneration and to a consequent opening of blood-vessels, with transport of cartilage cells.

Osteoma.—Tumors composed of bone arise from preexisting bone or cartilage. In children they may occur in the form of multiple exostoses of the skeleton, a condition similar to ecchondrosis, as which the former condition may begin. Exostosis also appears to be a developmental anomaly, and like ecchondrosis may show an hereditary or familial tendency. A less generalized form of osteoma may involve the bones of the skull, occurring particularly about the orbit or upon the frontal bone, and leading sometimes to marked deformity, as in two cases reported by v. Eiselsberg.[61] The growth may begin at or shortly after puberty, and is slowly progressive. Bony tumors of the kinds mentioned are usually outgrowths of the surface of the bone and arise from periosteum or perichondrium. In rare instances, tumor-like masses of dense bone may be present within the shaft of a long bone, arising apparently from the endosteum or the bone forming cells within the medullary cavity.

The osseous tissue of osteomas may be dense and compact, like the cortex of normal bone, or it may have the structure of spongy bone. In either case the bony lamellæ and the canal systems are less regularly arranged than in normal bone. Benign tumors containing bone often contain also cartilage and fibrous tissue, and may then be termed osteochondrofibromas.

Melanoma.—Benign excess anomalies rich in pigment cells constitute the common pigmented moles or nevi of the skin. They are maldevelopments and not, in the strict sense, blastomas, although they may give rise to highly malignant tumors. An extreme example of congenital pigmented mole is the bathing-trunk type, a case of which was reported by Fox[62] in 1912 in a girl 4½ years old (Fig. 301), and more recently by Quigley[63] in a young man of 24 years. There is still controversy as to whether the pigment is formed primarily by specialzied mesoblastic cells, the chromatophores or melanophores, or by the epithelium. Certainly in some of the lower animals the pigment forming cell of the integument appears to be a highly specialized, often amoeboid or contractile cell of the sub-epithelial tissue. A study of the dermal chromatophores some years ago by the writer[64] led to the conclusion that these cells in the human skin are also specialized mesoblastic elements whose function is the formation of pigment. Observations by others, which would localize the active pigment formation in the epithelium and would make the pigmented cells of the dermal stroma ordinary phagocytic cells which have become secondarily pigmented, do not appear convincing. This is particularly true in view of the occurrence of branching, pigment containing cells of the chromatophore type in the dura, cells which may occasionally give rise to malignant malanoblastomas of the meninges. Under normal conditions these cells may be so numerous that it is sometimes possible to distinguish the brain of the negro from that of the caucasian by the greater pigmentation of areas of the dura of the former.

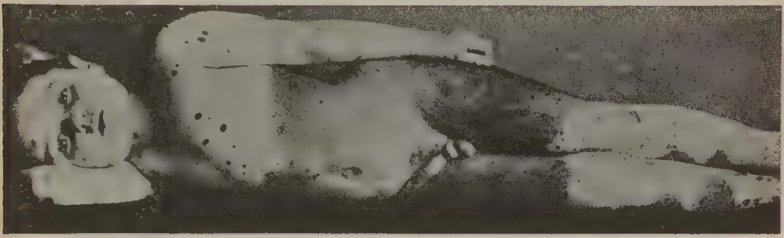

Fig. 301.—Bathing-trunk type of congenital pigmented mole; girl aged 4½ years. (Fox.[62])

The pigmented mole may vary in color from light brown to black, depending upon the richness of the tissue in pigment cells. In addition to the latter, the other elements of the skin may be hyperplastic. The mole may be covered with hair, the sebaceous glands may be prominent, and the epithelium may be thickened. The frequent association of hypertrichosis and anomalies of pigmentation with neurofibromatosis has been referred to above. Kawashima,[65] who reported a case of v. Recklinghausen's disease with a tumor of the adrenal medulla, and Saalmann,[66] who described a case of neurofibromatosis with primary hypernephroma of the liver, both believed that adrenal involvement may be an essential element in v. Recklinghausen's disease and may be a factor in the pigmentation which is so frequent in this condition. There does not, however, seem to be much evidence which would implicate the adrenals in the anomalies of pigmentation either of neurofibromatosis or of moles.

Angioma.—The angiomas, like the pigmented moles, are often simple developmental errors rather than progressively growing neoplasms. In many instances, however, although they may be maldevelopments already present at birth, they increase in size quite considerably and rather rapidly immediately after birth or sometimes at puberty. Unless malignant transformation occurs, they tend finally to reach a stationary condition. Poor delimitation at the margin often gives them the appearance of invasion, and their presence may lead to atrophy of the tissues in which they occur. Two main kinds of angioma are recognized; the form composed of blood-vessels filled with blood, hemangioma, and that made up of lymph vessels filled with lymph, lymphangioma.

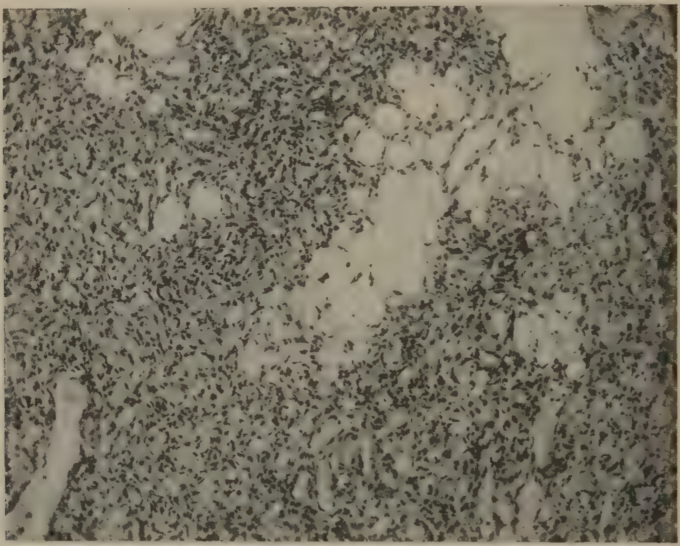

FIG. 302.—Racemose hemangioma of skin and subcutaneous tissue. ×140.

Hemangioma.—The hemangiomas, in turn, may be divided into two groups, depending upon the structure of the blood-vessels which make up the tumor. The first of these is the racemose hemangioma, the second the cavernous hemangioma.

Racemose Hemangioma.—The racemose hemangioma is composed of vessels of small calibre and usually of precapillary arteriolar type (Fig. 302). Their walls may be fairly distinct and may contain smooth muscle. The vascular lumens are lined by prominent endothelium. The content of the vessels in blood may vary at times during life, the hemangioma, when present in the skin and subject to direct examination, at some times being paler and at other times deeper red in color. Because of the escape of blood and the collapse of the vessels when the vascular complex is removed, the tissue may have a cellular structure in which many of the vascular lumens can not be seen.

This is the form of hemangioma seen so frequently in the skin as the strawberry birth-mark or vascular nevus, often involving large areas. The skin over the nevus may be hypertrophic. The congenital character of this form is illustrated by Kramer's[67] series of 147 hemangiomas in children, in whom the lesion was present at birth or appeared shortly thereafter. Of this series 29 per cent. were boys and 71 per cent. girls. The congenital or early origin is apparent also in the statistics of Fitzwilliams,[68] who found that in 83 per cent. of 645 patients the hemangioma had been observed at birth, and in an additional 13 per cent. it appeared within the first three years of life. The greater preponderance of the lesion in females is borne out by a tabulation of 1647 cases made by Stewart and Bettin[69] from the statistics of German and British authors; of this large group, 66 per cent. were girls and 34 per cent. were boys. They gave the regional distribution in 646 cases as follows: Face and neck, 56.8 per cent.; trunk, 24.9 per cent.; extremities, 17.5 per cent. Patton[70] found that 16 per cent. of 108 cases of hemangioma gave a history of the familial occurrence of the condition. Babington,[71] in 1865, described a condition of familial capillary telangiectasis of the nasal septum, characterized by profuse and repeated hemorrhage. Steiner,[72] who reviewed this rather striking clinical entity in 1917, found a record of the occurrence of the condition in as many as five generations.

Cavernous Hemangioma.—The cavernous hemangioma consists of wide, sinus-like blood spaces, which are lined by flattened endothelium and are separated from each other by relatively thin, fibrous septa. A small amount of muscle may at times be present in the latter. The cavernous hemangioma is usually surrounded by a fibrous capsule, and is not so apt to increase in size immediately after birth as is often the case with the racemose variety. The cavernous form is usually interpolated between an arteriole and a venule and appears then to represent a malformed, hypertrophied and dilated capillary bed. At times this vascular anomaly appears to be, not a neoplasm or even a congenital maldevelopment, but a simple ectasia of capillaries and venules in an area from which the original intervascular tissues have disappeared. This is the case especially in the liver of adults, one of the frequent sites of cavernous hemangioma. The condition is often present in the liver in children, however, and then appears to be the result of an anomaly of development (Schmieden[73]).

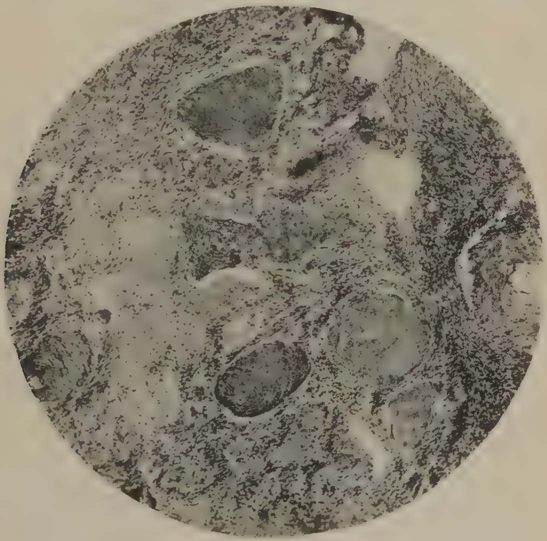

FIG. 303.—Cavernous hemangioma of ileum. ×80.

The hemangiomas may assume considerable clinical importance either because their presence in the skin may lead to marring of the appearance or because their occurrence in other situations may be associated with clinical symptoms brought about mechanically by the neoplasm. In the brain or meninges, where racemose hemangiomas are not rare, the manifestations may be those of brain tumor or of epilepsy, the latter often of the Jacksonian type. In Lechner's[74] tabulation of 57 angiomas of the brain and meninges, the condition occurred ten times in children. In two of these cases the meningeal hemangioma was associated with angioma of the face. Cushing[75] has noted, as a peculiar symptom of hemangioma of the skull, widening of the palpebral fissure of the side of the lesion, with a peculiar blue color of the sclera. In the intestine, where the hemangioma is of the cavernous type, it may be localized and polypoid, and may lead to invagination of the intestine with obstruction. Sussig[76] has reported such a case in a three months old girl, the angioma being situated in the lower portion of the ileum. We have recently seen a similar case in a young girl, in whom intestinal hemorrhages, continued over a long period of time, had led to a marked degree of secondary anemia; the hemangioma (Fig. 303), which was located in the lower portion of the ileum, finally led to invagination of the intestine and to symptoms of obstruction. In his group of 55 cases of intestinal obstruction in 53 children, Peterson[77] included a similar tumor. In Kausch's[78] case, a 16 year old boy, there had been repeated hemorrhages since the first year of life, which had led to several operations for supposed congenital hemorrhoids. Extirpation of the rectum showed the latter to be the seat of diffuse cavernous hemangioma throughout its entire extent. Some of the vascular spaces were thrombosed and others were calcified. Brown,[79] who has made the most recent compilation of vascular tumors of the intestine, described a diffuse cavernous hemangioma of the upper jejunum in a girl aged 12 years. Slight abdominal distress was followed by sudden intestinal obstruction. Death occurred two days after resection of the involved portion of the intestine. Brown tabulated nineteen cases of vascular tumor of the intestine from the literature, but he failed to include the cases of Kausch aud Sussig. His table includes a hemangioma of the rectum in a girl aged 10 years, in whom there had been repeated intestinal hemorrhages since the age of two years; an encircling hemangioma of the intestine in a woman aged 21 years, with symptoms due to the lesion since childhood; and a case with two small, circumscribed hemangiomas of the sigmoid of a man aged 37 years, who had had recurrent intestinal hemorrhages since the age of seven years.

Cavernous hemangioma of the urinary bladder is rare; when it occurs it may lead to hematuria. We have recently seen such a condition in an adult, in whom large, repeated and uncontrollable hemorrhages resulted in death. Langhans,[80] in 1879, had reported a similar condition in a boy of 19 years, who had had periodic hematuria since the age of nine years; death resulted from a final hemorrhage lasting 10 days. In the larynx, cavernous hemangiomas are fairly frequent. Kramer and Yankauer,[81] with 14 cases of their own, have brought the total of reported cases to 89. Their own cases were all adults, in whom the condition is much more frequent than in children. In the former the angioma is usually small and situated on the vocal cords. In children it is larger, more diffuse and subglottic.

Hemangioma of the bones is comparatively rare. Hitzrot[82] was able to collect only 28 cases in 1917; two additional cases have been reported, one by Cushing[75] and one by Ewing.[18] The distribution of these 30 cases was as follows: Skull, 16; extremities, 8; vertebral, 6. Hitzrot recognized three types of hemangioma of bone: The solitary angioma, the group to which practically all the reported cases belong; multiple angioma with a similar lesion in another organ; and multiple primary hemangioendothelioma. When it occurs in the joints the hemangioma may lead to destruction of cartilage and bone. Haas[83] reported such a case and found nine additional cases of hemangioma of joints in the German literature.

In the spinal cord and its coverings the condition may give rise to symptoms of cord tumor. Cobb,[84] who reported a case in 1915, found seven previously reported examples. Hemangioma of the peripheral nerves may lead to deformity of the involved limb. In the case reported by Stewart and Bettin,[69] a boy aged 10 years, the hemangioma involved the sciatic nerve and its branches. Nodular swellings of the leg made their appearance when the child was 10 months old, and became associated finally with such a degree of pain and flexion deformity of the knee as to necessitate amputation.

Schuster[85] reported a cavernous hemangioma of the heart in a new-born child, the lesion being in the wall of the right ventricle. The cardiac hemangiomas are usually only a millimeter or two in diameter and are not infrequently encountered in the heart valves of young infants. Lowenburg[86] reported a unilocular hemangiomatous cyst of the liver in a male child 19 months old; drainage of the cyst was followed by the continuous escape of serum, progressive weakening and death; the escape of serum rather than of blood leads one to suspect that this may have been a cystic cavernous lymphangioma. Simonini[87] has recorded a cavernous hemangioma which occupied two-thirds of the right lobe of the liver; rupture led to the death of the child at the age of 12 days. Rarer localizations of cavernous hemangioma are the striated musculature of the tongue and of the extremities. An erectile hemangioma of the umbilicus in a child six months old, reported by Chassaignac, and one in a new-born infant, reported by Lawton, are mentioned by Cullen.[88]

Lymphangioma.—Lymphangioma as a congenital neoplasm is of the cavernous type. There occurs also a lymph vessel neoplasm composed of solid cellular cords derived from the endothelium of lymph channels, but this belongs more properly under the lepidic tumors than under the hylic ones.

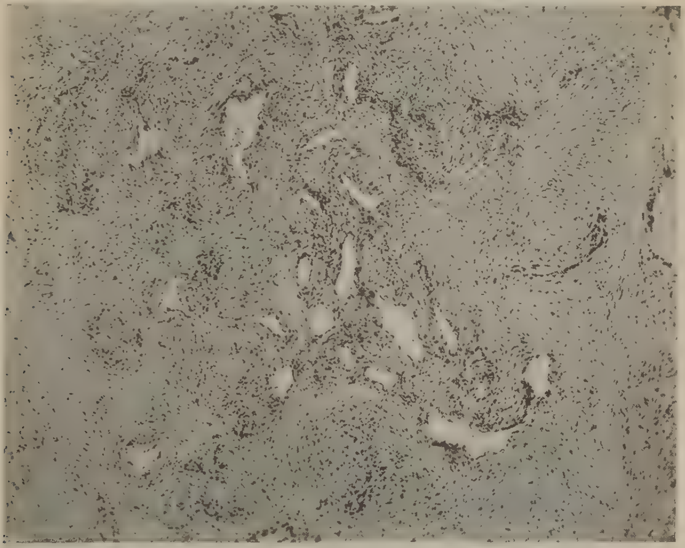

FIG. 304.—Fibrous cavernous lymphangioma of skin. ×80.

The cavernous hemangioma is often present at birth or manifests itself shortly thereafter. It consists of wide, sinus-like, lymph filled, endothelial lined spaces which are embedded in fibrous stroma (Fig. 304). The latter may contain smooth muscle or follicles of lymphoid tissue. The tissue between the lymph spaces does not usually form such distinct and thin septa as characterize the cavernous hemangioma, and the lymphangioma is usually less sharply circumscribed or encapsulated than the corresponding hemangioma (Fig. 305). The former, may, therefore, appear suggestive of infiltrative growth at its periphery, where new formation of vessels by the outgrowth of solid endothelial buds may be seen. This fact explains the tendency to recurrence after removal. Increasing distension of the lymph spaces may lead to coalescence of the latter, with the formation of large, cystic, tumor-like masses which are situated most often in the neck (Fig. 306) and may be bilateral. Such hygromas, because they occur most often at the sites of fusion of certain of the embryonic fissures, have been termed fissure hygromas. Thin walled cysts of the mesentery, usually unilocular but sometimes multilocular, filled with chyle or lymph, may be congenital. Shukowsky[89] reported the presence of three small cystic lymphangiomas in the liver of a new-born girl. In their cystic

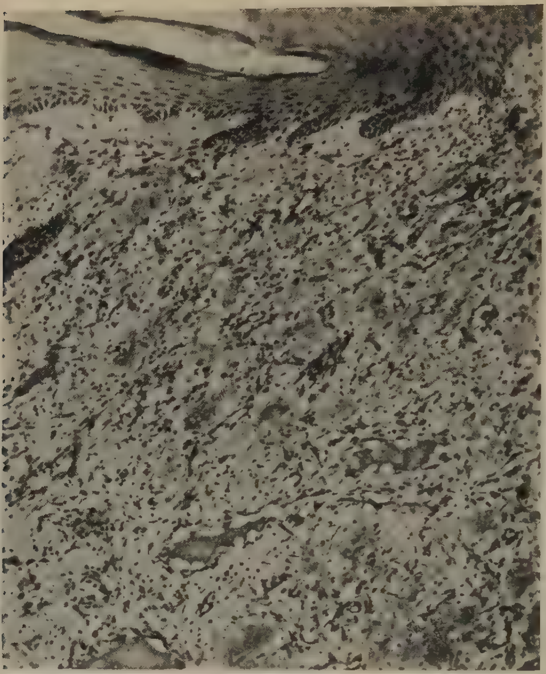

FIG. 305.—Cavernous lymphangioma of scalp, showing absence of delimitation toward the epidermis. ×140.

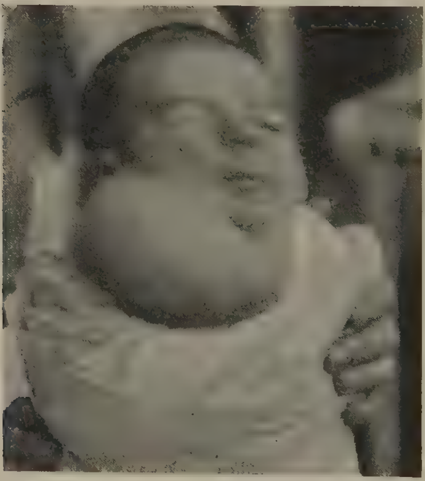

FIG. 306.—Cystic hygroma of neck. (Collection of Dr. I. A. Abt.)

character these lesions of the mesentery and liver are like the hygromas, and they usually appear to be simple malformations without any excess formation of lymph vessels.

In the tongue and lip the lymphangioma is usually quite diffuse and may cause marked enlargement and deformity of the tongue (macroglossia) or of the lip (macrocheilia). The lymph channels are cleft-like, with well defined walls, and are embedded in the striated musculature. Merkel[1] described a recurring lymphangioma of the thoracic wall in a two year old boy, associated with a diffuse lymphangioma of the spleen.

Hylic Blastomas of Epiblastic Origin

The epiblastic derivative which normally has a hylic character is the nervous system. The benign tumors which may come from this hylic tissue are the ganglioneuromas, the gliomas, the neurinomas, and the chromaffinomas. These have been discussed in detail above and require no further consideration at this point. Each of these varieties of tumor may become malignant.

Hylic Blastomas of Hypoblastic Origin

Chordoma.—The only hylic derivative of the hypoblast is the notochord. This has usually disappeared by the time of birth, except for vestiges embedded in the intervertebral discs. Misplacement of notochordal tissue may occur; such misplaced masses may grow progressively and form tumors of a benign, non-infiltrative character, chordomas; or they may form rapidly growing, infiltrating, malignant tumors, chordoblastomas. The chordoma is composed of mucoid tissue which has somewhat the appearance of myxochondroma, under which the chordoma was included by Virchow with the name ecchondrosis physalifora. The cells are large and epithelioid in character; their outlines may be indistinct, giving the tissue a syncytial character (Fig. 307). The matrix is usually vacuolated. Misplacement of chordal tissue has been observed most often at the clivus of the base of the skull, where the resulting tumor is subdural, and in the sacro-coccygeal region, where the tumor may be situated either anterior or posterior to the sacrum. Misplacement in the cervical region has also been described. An unusual situation for chordoma is the jaw; Koritski[90] reported such a case in a child aged six weeks,

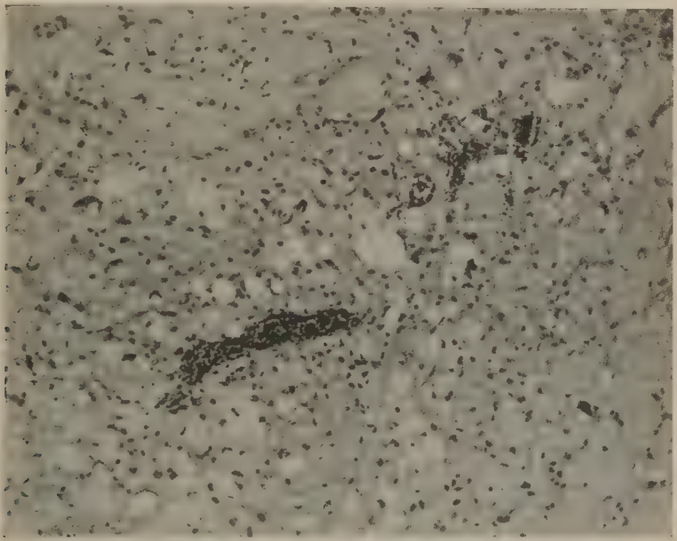

Fig. 307.—Chordoma of vertebral column. ×140.

the tumors being situated in both upper and lower jaws. They were pedunculated and were covered by buccal mucosa. Benign chordoma is a rare neoplasm and is extremely infrequent in children. Stewart's[91] tabulation, made in 1922, included only the case of Koritski. Merkel[1] mentioned another case in a boy aged 16½ years.

BENIGN LEPIDIC BLASTOMAS

Papilloma.—The benign lipidic tumors arise from surface or glandular epithelium, or from endothelium or mesothelium. Such tumors of surface epithelium usually exaggerate the normal relation of epithelium to stroma, both of which are hyperplastic. The stroma forms slender, often branching, finger-like processes, which give to the structure its name of papilloma. The epithelium is thicker than normal, but tends to retain its normal characteristics. It does not penetrate below the level of the original epithelial surface. The epithelium which gives rise to papilloma may be the hornifying squamous epithelium of the skin, the transitional squamous epithelium of the upper air passages and of the genitourinary tract, the columnar epithelium of the respiratory and intestinal tracts, and the cuboidal neuroepithelium of the ventricles of the central nervous system. In any of these situations the papilloma may be congenital, or it may arise after birth, often upon an inflammatory basis.

The papilloma of the skin may occur as wart-like growths, or as larger, fungoid, cauliflower-like masses. Such large tumors, because of constant trauma to which they are subjected, may become malignant. In the intestine a papillary surface arrangement may be associated with the formation of glandular structures; pure intestinal papillomas are less frequent than pedunculated polypoid tumors with a purely glandular character. Both forms are often congenital, and may show a tendency to familial occurrence. In the urinary tract, papillomas may be situated in the bladder, ureter or renal pelvis. They frequently lead to hematuria. Thomas[92] has reported a papilloma of the pelvis of the kidney of a girl aged 3½ years; the tumor did not invade deeply and appeared to be only moderately malignant, but led to death from early recurrence. Saelhof[93] reported a benign papilloma of the eye in a boy aged eight years. The tumor, which arose from the ciliary body filled the posterior chamber. This tumor is probably to be grouped with the papillary neuroepitheliomas of the eye and of the ventricles of the brain. Papilloma of the larynx, while not a common condition in children, is of clinical importance because of its great tendency to recurrence after removal. Chiari[94] gave the incidence as 10 cases in 7324 children under 10 years of age, and Clark[95] one in 1000 children under 14 years of age at the Massachusetts General Hospital. The tendency to recurrence is illustrated by the case reported by Ullmann.[96] The patient, a boy who began to complain of hoarseness at the age of three years, had been subjected to four successive operations because of recurrence within the space of three years. Death finally resulted from bronchopneumonia, and at necropsy the larynx and trachea were filled with papilloma down to the tracheal bifurcation. Crowe and Breitstein[97] say that in children under five years of age papilloma of the larynx has a mortality equal to or greater than that of carcinoma of the larynx in adults.

Adenoma.—Benign tumors originating in glandular epithelium are characterized by the formation of glandular acini or lobules which usually reproduce fairly closely the normal structures from which the tumor has arisen. So long as the tumor remains benign the epithelium is well differentiated and is sharply delimited from the surrounding stroma.

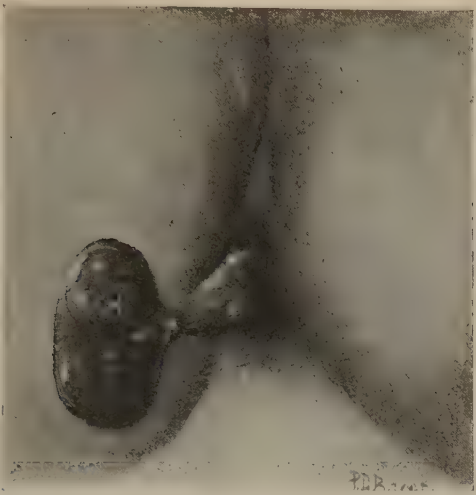

FIG. 308.—Prolapsed rectal polyp. (Collection of Dr. I. A. Abt.)

The most frequent example of adenoma in childhood is the glandular polyp of the intestine. While such polyps may occur anywhere in the tract, they are most often situated in the rectum. They are pedunculated (Fig. 308) and are composed of cellular, lymphoid stroma in which the glands, lined by single layered columnar epithelium, are embedded (Fig. 309). Twisting of the pedicle may lead to spontaneous amputation of the polyp. Peterson's[77] series of cases of intestinal obstruction

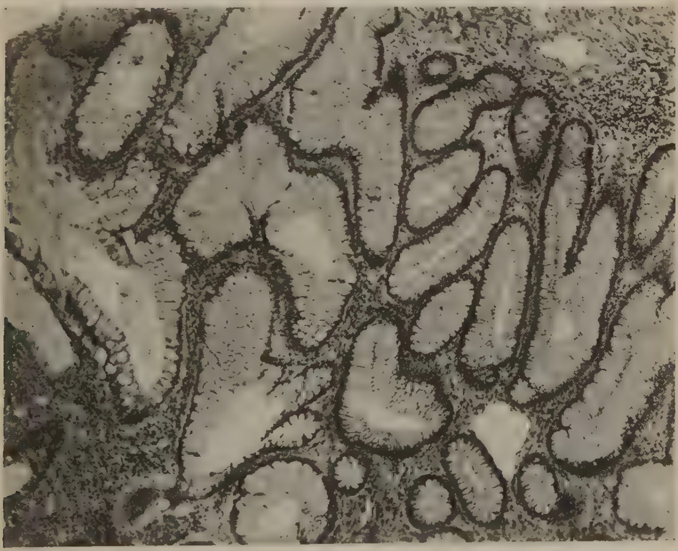

FIG. 309.—Glandular rectal polyp; girl aged 2¾ years. ×90.

in children included one due to a cyst-adenoma of the ileo-cecal region in a child aged 6½ months.

Fraenkel,[98] in 1892, was apparently the first to apply the term macrocheilia to enlargement of the lip due to an hyperplastic and adenomatous condition of the labial mucous glands, as opposed to the macrocheilias due to inflammatory processes and to lymphangioma. In his case, a boy aged 19 years, the condition had been present since the age of four years. Eisendrath[99] reported a similar case in 1904, both lips being involved in a boy aged 16 years; the enlargement was first noticed when the patient was 10 years old. Hatton,[100] who reported a case in an adult in 1920, collected thirteen previously reported cases. All of these and his own were males and in all the condition had begun during childhood; in one it had been present since birth. In the total 14 cases, the upper lip was involved nine times, the lower lip three times, and in two cases the condition was present in both lips. It is apparently a congenital excess formation of mucous glands, with later adenomatous hyperplasia. The peculiar adenomatous lung structures reported by Linser,[101] Zipkin,[102] Muus,[103] and Björnsten[104] as embryonic maldevelopments of the lung have already been described in Tumors of the Lung (Chapter LXV, Volume IV, page 53). Small, localized adenomas composed of cortical renal tubules (Fig. 310) and situated in the cortex of the kidney may be looked upon as local congenital excess anomalies, or hamartomas in the sense of Albrecht.

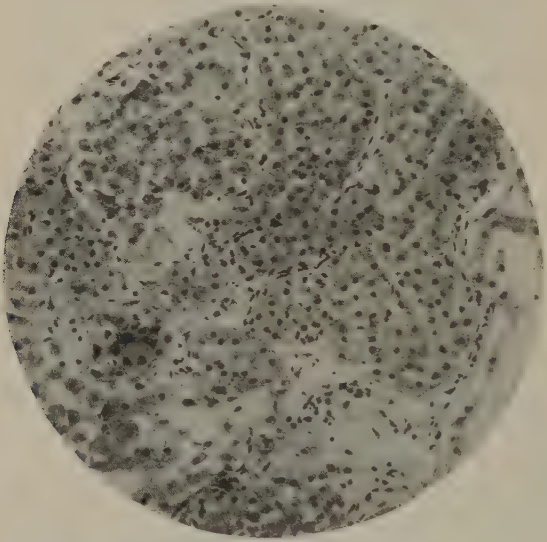

FIG. 310.—Adenoma of cortex of kidney. ×170.

Adenoma of the liver is believed to arise from sequestrated islands of liver tissue which lost their normal relationships to the rest of the liver during fetal development. Such hepatomas are usually encapsulated. They are composed of cells like those of the liver parenchyma, but liver cords and lobules are rarely formed and interlobular bile ducts are absent. Many of the cells may be vacuolated. Bile capillaries may be formed, and the cells apparently have the property of forming bile. The tumor itself may be deeply bile pigmented, but systemic jaundice is absent. Such a tumor has been described by Milne[105] in a six months old infant. Shaw[106] reported a hepatoma of the right lobe of the liver of a boy aged 13 years, which measured 15.5 by 12 cm. and weighed 2 lb., 3 oz. The boy was alive and in good health 20 months after removal of the mass. The liver cell adenoma may become atypical and show other evidence of malignancy, such as secondary nodules within the liver, tumor masses in the portal or hepatic veins, and metastases in distant organs. Shaw collected 22 examples of this tumor from the literature, of which 45 per cent. were in males. Small subcapsular adenomas derived from the interlobular bile ducts have also been encountered in children, but are rarer than the hepatomas.

In the thyroid there may occur encapsulated adenomas composed of undifferentiated fetal thyroid tissue. These may be present at birth. Tumor-like nodules of thyroid tissue may be situated at the root of the tongue, in the region of the thyro-glossal duct. These are the result of misplacement; their size is at times apparently due to compensatory hypertrophy as the result of congenital absence or maldevelopment of the thyroid itself.

The umbilicus may be the seat of reddish, tumor-like, polypoid outgrowths of variable size, to which the name adenoma has been applied. Küstner[107] and Kolaczek,[108] in 1877, each described two cases in young children. Küstner at first believed that such structures are derived from remnants of the urachus, but was led by the study of his second case to conclude that they come from persistent rests of the omphalomesenteric duct. Kolaczek, also convinced by the similarity of the epithelium of the umbilical adenoma to that of the crypts of Lieberkühn, likewise accepted an origin from the omphalomesenteric duct; he termed the lesion an enteroteratoma. Later writers have emphasized the similarity of the covering tissue of the polypoid masses to intestinal mucosa, and have believed that they are the result of persistence of the outer end of the duct, although a few have maintained an origin from the urachus or from misplaced peritoneal mesothelium. Waegeler,[100] from the study of a case in an adult, concluded that the umbilical adenoma comes from misplaced remnants of the upper part of the primitive urogenital system. Cullen,[88] in 1916, collected from the literature 39 examples of the lesion in children, confirmed by microscopic examination, and a few others in which no microscopic examination was made. He objected to the use of the term adenoma and proposed umbilical polyp. The frequent association of the anomaly with Meckel's diverticulum or with a fibrous cord which represents the omphalomesenteric duct is to be borne in mind when removal of the umbilical polyp is proposed.

With the adenomas may be included the adamantinomas and solid or partly cystic epithelial tumors of the jaw derived from the enamel organ of the teeth. Such tumors may occur early in life or may be present even at birth. Schlosser[111] credited Coote with a case in a child aged six months and Wilke with a polycystic adamantinoma of the jaw in a newborn child. Massin[111] reported the occurrence of two submucous polypoid tumors of the gum in a newborn child, which were composed of large epithelial cells believed to have come from the tooth anlage. The tumors were considered benign; they did not recur after removal. Moschcowitz[112] reported a pigmented odontoma of the jaw in a child 4½ years old; the tumor had been present since the age of six weeks and had increased gradually in size.

Cysts.—Cysts derived from certain fetal structures, like the thyroglossal duct, the branchial clefts, and Rathke's pouch, may at times be associated with hyperplasia of their epithelial linings, which may be papillary, adenomatous or solid. The proliferating squamous epithelium of Rathke's pouch cyst may be transformed into putty-like, cholesteatomatous material. Three cases of dermoid cyst of the floor of the mouth, believed to be due to ectodermal misplacement at the time of the closure of the first and second branchial clefts, have been reported by Colp.[113] One of these, in a woman aged 21 years, was first noticed at the age of eight years, and another, in a girl aged 15 years, had been present for two years. The cysts were lined by squamous epithelium, beneath which were sebaceous glands. Colp abstracted from the literature 32 cases of dermoid cyst of the floor of the mouth. In five of these the microscopic structure was such as to indicate that the cysts were of duct origin, and in nine no microscopic examination had been made. Of the remainder, five occurred in children or had been present since childhood. Cysts due to misplacement of the epidermis, often termed sebaceous cysts but more properly epidermoid cysts, may be filled with similar material. Similar so-called dermoid cysts, composed only of a fibrous wall with an inner epidermal lining, may occur in the mediastinum or in the connective tissue of the pelvis, apparently as the result of misplacement of epiblastic tissue fairly well along in its differentiation to epidermis. Of 25 extra-ovarian, simple, pelvic dermoids tabulated by Germain,[114] all but three were in women, and the youngest patient was aged 18 years at the time of observation.

Cysts of the ovary, a not infrequent lesion in very young girls, may contain papillary ingrowths. Hubert,[115] who collected 200 tumors of the ovary in girls up to the age of 15 years, found 35 per cent. to be cysts. Wiel[116] found 32 per cent. of 60 cases of ovarian tumor in children under 10 years of age or younger to be cysts. Downes,[117] who reported a large cyst of the ovary in a child seven months of age (Fig. 311), found only two cysts among the 26 additional cases of ovarian tumor in girls under 10 years of age reported since the time of Wiel's communication.

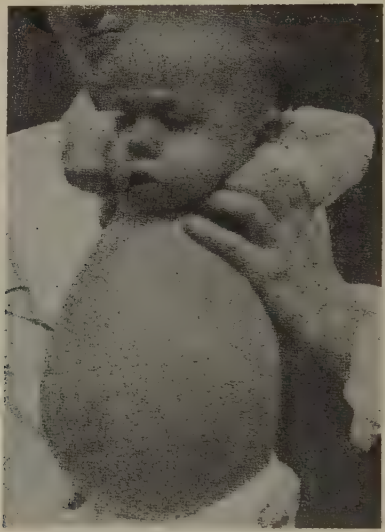

FIG. 311.—Abdominal enlargement due to cyst of ovary in a child aged 7 months. (Downes.[107])

Endothelioma.—The usual type of benign endothelioma is the lymphangiomatous wart or papilloma of the skin to which the name lymphangioma hypertrophicum has been applied. It is composed of solid, cord-like or alveolar masses of small polyhedral cells with rather deeply stained nuclei (Fig. 312). The cells are derived from the endothelium of lymph vessels.

Carcinoid.—Among the benign lepidic tumors we may place the so-called carcinoid, which may occur in the small intestine, the appendix or Meckel's diverticulum. The tumor is usully small, sharply defined in the gross, and light yellow in color. Microscopically it is made up of solid alveoli of closely placed polyhedral cells whose outlines are indistinct (Fig. 313). The cytoplasm may be vaculoated. The nuclei are relatively large and vesicular. The cell nests vary in size and in shape. Microscopically the tumor tissue is not so well delimited as in the gross and the distribution of alveoli at the periphery may be suggestive of invasion (Fig. 314). The larger cell masses may contain sinus-like blood spaces, which, together with the cellular morphology, give a picture at times strikingly like the islands of Langerhans of the pancreas. Carcinoid of the appendix as a rule has been

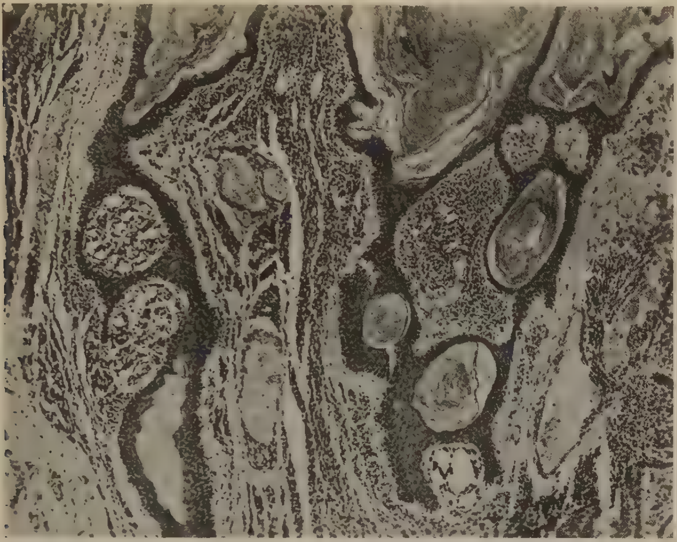

Fig. 312.—Lymphangioma hypertrophicum (benign lymphendothelioma) of skin. ×80.

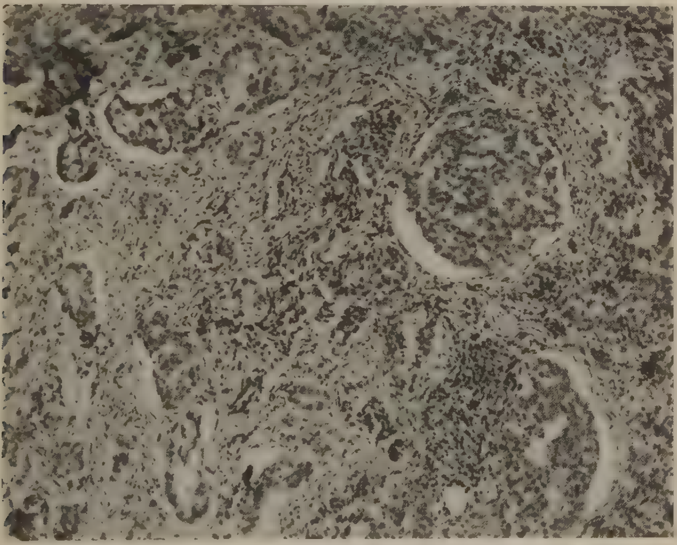

Fig. 313.—Carcinoid of appendix; tumor alveoli in the obliterating fibrous tissue of the lumen. Girl aged 12 years. ×140.

encountered at an average earlier age than that of the small intestine. Hicks and Kadinsky,[118] who in 1922 reported a carcinoid tumor of an acutely inflamed and perforated Meckel's diverticulum in a boy aged

12 years, claimed that this was the first reported example of such a tumor in a diverticulum. In the appendix, where the mass is situated at the tip and obliterates the distal end of the lumen, it usually gives rise to no symptoms, but is a chance finding in an appendix removed because of inflammation, evidences of which are present in the mucosa proximal to the tumor. Such was the case in the appendix from which Figs. 313 and 314 come, removed from a girl aged 12 years because of symptoms of acute appendicitis; an acute, ulcerative inflammatory process was present in the mucosa above the tumor.

Concerning the nature and origin of the intestinal carcinoid there has been considerable discussion and not a little controversy. Older reports referred to the tumor as a carcinoma or epithelioma, or more rarely as a lymphendothelioma. Even so late as 1917 Kirmisson[119] reported as an epithelioma a typical example in an acutely inflamed, perforated appendix removed from a girl aged 14 years; there had been no recurrence after two years. The absence of recurrence, which is the rule after the simple appendectomy which reveals the mass, established the clinically benign character of the lesion in the great majority of instances, and it has been necessary for the pathologist to revise his opinion in regard to those microscopic features which he had considered evidence of invasion. Oberndorfer[120] appears to have been the first to suggest an origin from misplaced pancreatic tissue, a view accepted by Albrecht, Heller and Weigert in the discussion which followed his presentation. Toenniessen[121] also believed the carcinoids to be the result of misplacement and concluded that they are developmental anomalies rather than true tumors. Of more recent writers, Saltykow[122] has been the strongest proponent of the pancreatic origin. Pancreatic misplacement into the intestinal tract and into Meckel's diverticulum does occur apparently rather frequently. Usually such islands of misplaced tissue imitate closely the structure of the normal pancreas. Such is not the case with the carcinoid. If the latter is pancreatic in origin it must be homologized with the islet tissue, which it may closely resemble, and Saltykow maintained that the carcinoid is composed of islet tissue. It is rather difficult to

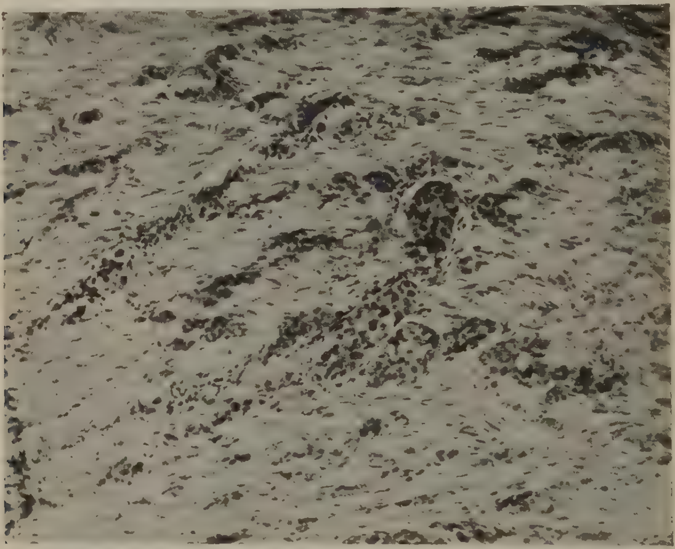

FIG. 314.—Carcinoid of appendix; apparent invasion of muscle coat. ×140.

understand why in the upper small intestine the misplaced tissue should give rise to typical pancreas, and in the appendix and lower small intestine only to islet tissue. It may be pointed out that Saltykow postulated three possibilities which might result from the further development of embryonic pancreatic tissue in the gastro-intestinal tract: First, the formation of typical islands of pancreatic tissue, encountered usually in the stomach and upper small intestine; secondly, islet tissue alone, resulting in the carcinoid of the appendix and lower small intestine; and third, pancreatic ducts alone, to which process he ascribed the formation of the so-called diffuse adenomyoma of the intestinal wall. The conception of Albrecht,[123] who accepted the pancreatic origin of the intestinal carcinoid, in regard to the choristomas, among which he placed the pancreatic misplacements, has already been discussed. If we can accept Albrecht's underlying conception, then it might be possible to grant that certain cell masses of the primitive gut which are going to differentiate along abnormal lines might produce typical pancreatic tissue and still other masses might produce islet tissue alone. Schober,[124] a pupil of Mathias, accepted the latter's[125] views in regard to the progonomas, and placed the carcinoids of the appendix among the progonomas of pancreatic origin.

Burckhardt,[126] who reported a study of six examples of carcinoid of the small intestine and one of the appendix in 1909 and six further cases in 1912, concluded that this lesion is absolutely distinct from adenomyoma, misplaced pancreas and other developmental anomalies, and that it is a true blastoma. He claimed to have traced the derivation of the tumor cells from the epithelial cells of the crypts of Lieberkühn, and therefore believed that the carcinoid should be included among the basal cell epitheliomas of Krompecher. He admitted that the carcinoid differs from the usual carcinoma or epithelioma by its generally benign character, but was convinced that some of the reported metastasizing tumors of the appendix and small intestine were of the type termed carcinoid by others. Burckhardt's claim that the carcinoid arises from the cells of the crypts is of especial interest in connection with the latest contributions to the subject by Danisch,[127] Masson,[128] and Hasegawa.[129] These investigators have claimed that the carcinoid cell is identical with and is derived from a specific type of cell which can be identified in the crypts of the small intestine and appendix by its property of becoming blackened by treatment with silver nitrate. This argentoffin cell Danisch believed to be derived from the sympathetic nervous system and to be closely related to or identical with the phaeochromocytes or chromaffin cells of the adrenal medulla and other paraganglia. In our hands the carcinoid cells have given the chromaffin reaction. Danisch's conception of the origin of the carcinoid is that the argentoffin cells proliferate as the result of chronic inflammation of the mucosa, penetrate the basement membrane, and take on blastomatous properties. Masson and Hasegawa also placed the carcinoids among the tumors of neurogenous origin.

In view of the wide divergence of opinion indicated by the above survey, the final decision must await further research. The application of special staining methods to perfectly fresh material may help in the solution of the question. For the present we can say only that the carcinoid is usually clinically benign and that its histologic characteristics are those of a developmental anomaly rather than of a true blastoma. This statement is not to be understood as precluding the possibility of the development of malignancy in what is usually a benign developmental anomaly, a process of which there are frequent enough examples in the highly malignant endothelioma which may arise from the hypertrophic lymphangioma, the melanoblastomas which may originate from congenital pigmented moles, or the hypernephromas which may arise from misplaced adrenal cortical tissue.

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MALIGNANT TUMORS

HYLIC BLASTOMAS

The malignant tumors of hylic origin constitute the great group of sarcomas. Subclassification of this group is advisable whenever determination of the cell type which has given rise to a particular kind of tumor is possible. In such subclassification, a nomenclature which indicates the cell type of origin is desirable.

In the usual terminology this indication of the origin of a malignant hylic neoplasm is given by using a compound word composed of sarcoma to which is prefixed the name of the tissue giving rise to the tumor. Objections to this nomenclature are that it results in unwieldy terms, and that it does not sufficiently emphasize the fundamental differences in the great group of malignant hylic tumors, since it retains the name sarcoma for all. A nomenclature which would overcome the last named objection, which is a serious one, is one which would make use of names indicating that the tumors are composed of specific, young, formative cells. Such names have already been given us by the embryologists, who speak of the young cells which are to differentiate into adult tissues as blasts; thus we have erythroblast, lymphoblast, fibroblast, neuroblast, and a group of other words which indicate not only the immaturity of the cells but the kinds of tissue to which they give rise. If to such words we add the suffix "oma," indicating tumor, we have a group of terms which make known not only the immaturity and therefore the malignancy of the tumor tissues, but also the cell of origin of any given neoplasm. Such words will end in "blastoma," thereby introducing an element of confusion, since blastoma means any kind of tumor, whether benign or malignant, and since this broader meaning of the word forms the basis of some classifications already in use. Thus, Mallory,[1] for example, uses the term fibroblastoma to include both the benign fibroma and the malignant spindle cell sarcoma, myoblastoma to include both the benign myoma and the malignant myosarcoma, etc., a usage which results in no particular advantage from the introduction of the suffix "blastoma." If, however, we permitted only the suffix "oma" to indicate tumor, as it has done for so many years, and understood that the "blast" portion of the words we decide to use belongs to the root and indicates, as it should, a blast or formative cell, then the use of tumor names ending in "-blast-oma" would tell us that we are dealing with malignant neoplasms derived from specific cell lines, and for such neoplasms the name sarcoma could be discarded.

If we adopt this plan, in so far as possible, the benign tumor is an "oma" of differentiated tissue, the malignant tumor is an "oma" of young cells or blasts. Thus the benign tumor composed of adipose tissue is a lip-oma; the corresponding malignant tumor, composed of immature adipose tissue cells or lipoblasts, is a lipoblast-oma. We are not able to apply this system of nomenclature to every tumor, because we are not able in the case of every neoplasm to determine the cell type from which it arose. It is still necessary, therefore, to retain the term sarcoma for those tumors whose hylic character is apparent, but whose cells are so immature that we can form no definite conclusion as to their origin.

Classification of Malignant Hylic Tumors.—In accordance with the ideas expressed above, the following classification of the malignant hylic tumors may be made:

I. Tumors composed of totally undifferentiated cells: Sarcoma. (Borst's[2] "einfachsten Sarkome.")

1. Named according to cell morphology: Round-cell sarcoma. Mixed-cell sarcoma. Giant-cell sarcoma.

2. Named from the presence of tissue which differs from the actual tumor tissue: Myxosarcoma. Chondrosarcoma. Osteosarcoma.

3. Named from the arrangement of the tumor cells: Alveolar sarcoma. Perithelial angiosarcoma.

II. Tumors composed of partially differentiated cells: (Borst's[2] "höher entwickelten Sarkome.")

(*A*) Of mesoblastic origin

	Benign Hamologue
1. Myxoblastoma	Myxoma
2. Lipoblastoma	Lipoma
3. Fibroblastoma	Fibroma
4. Chondroblastoma	Chondroma
5. Osteoblastoma	Osteoma
6. Myoblastoma:	Myoma:
(a) Leiomyoblastoma	Leiomyoma
(b) Rhabdomyoblastoma	Rhabdomyoma
7. Melanoblastoma	Melanoma
8. Lymphoblastoma (including Lymphoid Leukemia and Leukosarcoma)	Lymphoma
9. Myeloblastoma (including Myeloid Leukemia and Chloroma)	Myeloma

(*B*) Of epiblastic origin	
1. Glioblastoma	Glioma
2. Neuroblastoma	Ganglioneuroma
(*C*) Of hypoblastic origin	
1. Chordoblastoma	Chordoma

MESOBLASTIC HYLIC TUMORS

Sarcoma.—The sarcoma, using this term for the present in its broadest sense, is the tumor of childhood and youth, as compared with the carcinoma, which is the predominating tumor of adult life. The tumors of the early years of life are not, however, exclusively sarcomas, and the preponderance of ordinary sarcoma over carcinoma in childhood is probably not so great as has been supposed. In the older literature the neoplasm which we now separate off from the general sarcoma group as the neuroblastoma appears always as a small round cell sarcoma. The same thing is true of other tumor groups, whose origin sharper precision of knowledge permits us to identify. Many so-called sarcomas of childhood undoubtedly develop in teratomas or mixed tumor. It is impossible, therefore, to form any exact opinion of the actual frequency of sarcoma in the early years of life. Warthin's[3] figures, already referred to, gave an incidence of 70 per cent. for sarcoma as compared with 13 per cent. for carcinoma. These figures probably give as close an approximation to the actual relative frequency as we may hope to arrive at from our present knowledge.

Round-cell Sarcoma.—If we adopt the plan of subclassifying the great group of sarcomas by using a specific terminology which indicates origin, then the term sarcoma would remain only for those hylic tumors which are composed of cells so immature that their origin can not be determined or so undifferentiated that it may be taken for granted that the tumor has arisen from the ordinary supporting tissue matrix which is present in all tissues and organs. This is the tumor usually termed round-cell sarcoma, and often further divided into small round-cell and large round-cell, depending upon the average diameter of the constituent cells. Of these, the small round-cell sarcoma appears to be the more immature. Differentiation from tumors derived from lymphoid tissue, lymphoblastomas, is exceedingly difficult and often impossible, upon morphologic grounds alone. The neuroblastoma and the glioblastoma are often so like the small round cell sarcoma that they have frequently been included with the latter.

The round-cell sarcoma is characterized by its great cellularity; by the small amount of stroma present, which occurs in the form of a fine supporting reticulum; by its thin walled blood-vessels; and by its early metastasis through the blood stream, and its consequent high malignancy. At times the resulting invasion of the body may be so widespread that the primary point of origin can not be determined and the condition must be put down as generalized sarcomatosis.

Since the small round-cell sarcoma originates from the supporting tissues, it may occur anywhere in the body, being most frequent in subcutaneous tissue, fascia, muscle and bone. In bone it may be multiple, and may apparently arise either from the periosteum or from the medullary tissue. Unusual localizations of round-cell sarcoma noted by Merkel[4] were the peri-anal tissues in a new-born child, the stomach of a girl aged 3½ years, and the parotid of a boy aged 12 years and one aged 2½ years. A round-cell sarcoma of the tongue, in a boy aged 17 years, and one composed of round and fusiform cells, in a boy aged two years, are included in Keenan's[5] tabulation of primary sarcomas of the tongue. Boschowsky,[6] who reported a case of primary sarcoma of the lung in an adult and collected 43 previously reported cases from the literature, included two examples of round-cell sarcoma of the lung in children, one a boy of 3½ years, the other a girl of two years.

Roy[7] has reported a round-cell sarcoma of the conjunctiva in a boy aged six years. A round-cell ring sarcoma of the iris was reported by Parsons;[8] the tumor occurred in a boy aged 14 years, in an eye which had been injured four years previously by a football. Walter (in Mönckeberg[9]) described a small round-cell sarcoma of the orbit, as large as a man's fist, present in a still-born child.

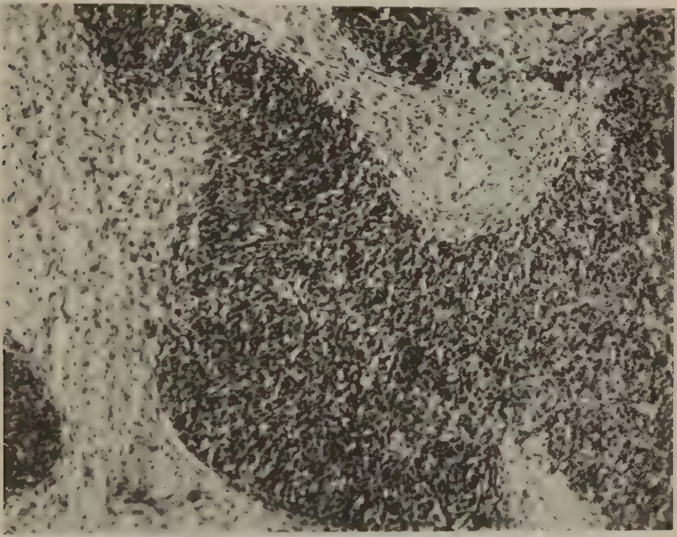

Fig. 315.—Retroperitoneal large round-cell sarcoma; boy aged 4 years. ×150.

Somewhat rarer localizations of round-cell sarcoma of bone are the mandible, as reported by Mummery[10] in an infant nine months old; and of the tenth dorsal to second lumbar vertebræ, as reported by Duprat[11] in a boy 10 years old; in the latter case the cord and meninges were not involved. Breinl[12] described a round and spindle-cell sarcoma which had destroyed the first lumbar vertebra of a six months fetus; the tumor was believed to have arisen in the dura. Clark described as a primary, congenital, round-cell sarcoma of the spleen in a boy of 15 months a tumor which Smith and Rusk[13] believed to be secondary. A similar tumor of the spleen of a boy aged 14 years, reported by Herczel, they also believed to be probably secondary. The older literature contains many examples of so-called round-cell sarcoma of the liver associated with a similar tumor of the adrenal, usually of the right side. These were probably all neuroblastomas. Tumors described as small round-cell sarcomas, without adrenal involvement, have been reported by Bossowski (in Mönckeberg[9]) in girls aged respectively 3 and 11 years, and by Baumann and Forbes[14] in an 11 year old girl. Tumors of the thymus are described both as round-cell sarcoma and lymphosarcoma. Rubaschow[15] collected 69 cases of tumor of the thymus from the literature previous to 1911. This group included 15 described as lymphosarcoma and 52 as small round-cell sarcoma;

of the latter, 23 occurred in children. Some of these also were probably lymphosarcomas and one hesitates to believe that all of these tumors arose from the thymus.

Round-cell sarcoma of the kidney has been reported by Grego[16] in an infant aged 18 months. The rare condition of diffuse bilateral round cell sarcoma of the kidneys has already been discussed in the chapter on tumors of the kidney (Chapter CI, Volume IV, page 966). Wilder's[17] tabulation of 50 cases of sarcoma of the urinary bladder included four small round-cell sarcomas in children, aged respectively three years (two cases), 4½ years, and 14 years; in two other cases, the children being aged respectively 2¾ and 3⅔ years, the tumor was composed of both round and spindle cells. In Sysak's[18] tabulation of 22 tumors of the prostate in children, there were four round-cell sarcomas. A round-cell sarcoma of the ovary in a girl 23 months old was recorded by Hayd,[19] and Riedl[20] described a cystic round-cell sarcoma of the ovary in a girl aged six years, in whom menstruation had begun at the age of four years. McFarland's[21] collection of sarcomas of the vagina included three round-cell sarcomas in girls under 17 years of age and six sarcomas of the botyroid type composed of both round and spindle cells. The few reported cases of round-cell sarcoma of the intestine in children were probably all lymphoblastomas and will be included under the tumors of that group.

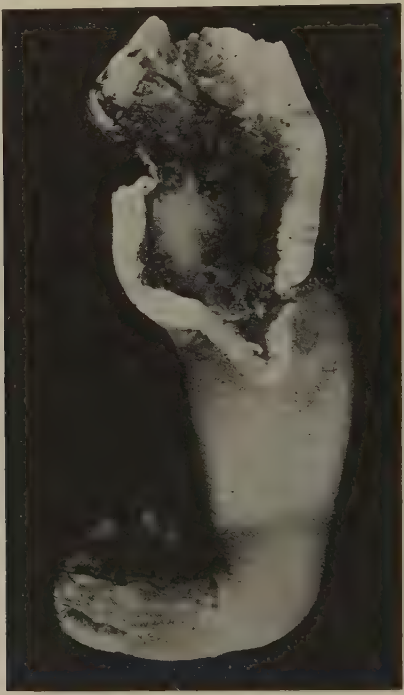

Fig. 316.—Recurrent round-cell sarcoma of arm in a girl aged 7 months.

A round-cell sarcoma of the skin of the forearm of a boy aged 2¼ years was reported by Ott[22] as an example of sarcoma following trauma. The tumor developed at the site of a dogbite within four weeks after the child was bitten. The writer has seen a round-cell sarcoma diffusely involving the plantar tissues of the foot of a child, which apparently followed a puncture wound of the sole caused by a nail. Other examples of round-cell sarcoma in whose origin trauma was believed to have played a part were reported by LeDentu[23] and by Latronche (Mönckeberg[9]). The first was a sarcoma of the vagina of a child aged 3½ years, which followed trauma to the lower abdomen. Latronche's case was a round cell sarcoma of the mesentery in a boy aged 11 years; a kick in the abdomen was supposed to have been a causative factor.

An unusual condition is that termed primary sarcomatosis of the meninges. The membranes of both the brain and cord are thickened, sometimes only slightly and at other times greatly, by a diffuse infiltration of tumor cells. The morphology of the latter in individual cases has varied from round to spindle cells, and in some cases the cells have had an alveolar arrangement. From the diversity of cell type it is probable that the condition may have a variable origin. The meningeal involvement is usually associated with hydrocephalus. Ford and Firor,[24] who have given a complete summary of the literature of meningeal sarcomatosis down to 1924, added 4 cases to the previously published 28. Two of their own cases occurred in children aged respectively 15 months and 10 years, and 15 of the previous 28 cases were in children. Of the 17 examples in children, 11 were males and 6 females. In the majority of these as well as of the entire group, the tumor was of the small round-cell variety and was termed round-cell sarcoma. In many cases the diffuse neoplasm of the meninges was associated with a subependymal tumor of a ventricle, which is to be considered the primary growth. These authors correctly conclude that most of the diffuse sarcomas of the meninges, spindle-cell as well as round-cell, are really malignant gliomas or glioblastomas.

Other Forms of Sarcoma.—While a strict limitation of the term sarcoma would reserve it for the most immature form of hylic tumor arising from indifferent supporting tissues, it may be advisable, in order to prevent confusion, still to use this term in connection with certain other hylic tumors characterized either by their cell morphology, or by some peculiarity of arrangement of the tumor cells, or by the admixture of other hylic constituents. Here it is usual to place the mixed-cell and certain giant-cell sarcomas, because of cell morphology; the alveolar sarcoma and the perithelial hemangiomsarcoma, because of the arrangement of the tumor tissue; and the myxosarcoma, chondrosarcoma and osteosarcoma, because of the admixture of mucoid, cartilaginous or osseous tissue.

Mixed-cell Sarcoma.—Many rapidly growing sarcomas are composed of both round and spindle cells. The growth rate is not as rapid as that of round-cell sarcoma, and the formation of spindle cells is probably the result of a sufficiently slow rate of division in some of the cells to permit partial differentiation. At other times the mixed character of the tumor is due to a sudden accession of growth energy in a fibrous or fibrosarcomatous tumor of previously slower growth; in such neoplasms the pleomorphism of the cells may be marked.

Giant-cell Sarcoma.—Pleomorphic sarcomas may contain giant cells in variable number. In some tumors the giant cells, often termed parenchymatous, belong apparently to the same lineage as the rest of the tumor cells. The increased cell size is apparently the result of disturbances of the intracellular division mechanism, due to hypernchromatism and an upset nucleus-plasma relation, as described by Howard,[25] and Howard and Schultz.[26] In other cases the giant cells are so strikingly like those of embryonic or regenerating muscle that origin of the neoplasm from muscle must be excluded if the tumor is to be included among the simple sarcomas. The pleomorphic, giant-cell sarcoma of the tunics of the testis of a boy aged 16 years, reported recently by Fischer and Wolters,[27] may be such a rhabdomyoblastoma rather than a simple giant-cell tumor. v. Bókay[28] has reported a giant-cell sarcoma of the ileum of a child nine months old; it was as large as an apple, was situated 1 m. above the ileocecal valve, and was composed of spindle cells among which were multinucleated giant cells. Zipkin[29] described a sarcoma of the subcutaneous tissue of the inguinal region of a male infant 18 weeks old, characterized by the presence of large numbers of giant cells of the Langhans type; he was convinced that the lesion was a neoplasm and not a granuloma. Joseph[30] described a congenital tumor of the abdominal wall of a girl aged five months, which was composed of small round cells with many giant cells. Odstrcil[30A] reported a case of multiple giant-cell sarcomas of the skin. The tumor nodules began to appear when the child was 14 weeks old and increased rapidly in number until 87 could be counted. The tumor tissue was composed of a mixture of polygonal, spindle and giant cells. No primary origin of the neoplasms could be discovered in the deeper tissues. Metastases were present in the kidneys, liver and muscles.

Giant-cell Sarcoma of Bone.—At the epiphyses of the long bones there occurs, especially frequently in young individuals, a peculiar condition characterized by enlargement of the end of the bone, bone destruction and bone formation, and the presence within the bone of a soft, spongy, dark red, often hemorrhagic mass. Cyst formation may be present. Microscopically the tissue is composed of a matrix of variable cellularity, in which are embedded numerous giant cells. The latter in general resemble the myeloplaxes of normal bone marrow. Concerning the nature of this lesion there has been and still is considerable discussion. Among modern pathologists the tendency is to consider the process not a true neoplasm, but a peculiar, perhaps inflammatory, granulomatous reaction on the part of the bone marrow, the giant cells being of the foreign body variety, rather than myeloplaxes. It is usually associated with hemorrhage, the latter often appearing to be the primary process. Those who deny the blastomatous character of the so-called giant-cell sarcoma of bone usually write this designation in quotation marks, and counsel conservative treatment. Of pathologists, Adami[31] entertains the possibility that the condition may be a true blastoma, derived from specific marrow elements, and terms it giant-cell myeloma. Many surgeons, as the result of clinical experience, are not convinced that the lesion is always a benign one, although admitting that simple curettage is enough to cure it in many instances. Coley[32] has recently summarized his experiences regarding the prognosis of giant-cell sarcoma of the long bones, based upon an experience with 50 cases. Recurrence, metastasis and death, frequently enough in spite of amputation, led him to believe that the opinion of pathologists that the lesion is a benign one must be modified, and that the malignancy can not be explained on the ground that the original diagnosis of giant-cell sarcoma in his series had been a wrong one. His series is important, not only because of the consideration that it deserves from the standpoint of prognosis, but also because it is large enough to illustrate the relative frequency of the condition in children. Of his 50 cases, the radius was involved in nine, none occurring in children. The humerus was the site of the tumor six times, and five of these cases were children varying in age from 6 to 14 years. In a humerus lesion of a six year old girl, included in the last group, there was no microscopic examination and the child remained well after roentgen-ray treatment alone; this may have been a bone cyst. There were 13 tumors of the tibia, 6 occurring in children aged 9 to 17 years. The femur led with 22 cases, of which 3 were in young people aged respectively 14, 16 and 17 years. If an opinion in regard to prognosis is to be expressed upon the basis of the microscopic examination, the character of the matrix in which the giant cells lie should receive chief attention. The ground substance may be quite cellular and composed of a tissue not to be distinguished from spindle-cell sarcoma. It is possible that in such examples the tumor may actually be a spindle-cell sarcoma, with all the attributes of the latter, and that the presence of giant cells, which may be the misleading feature, is a non-essential part of the process.

Giant-cell sarcoma may occur in the maxilla, mandible, and the vertebræ, as well as in the long bones. From the alveolar processes of the jaws there may develop tumor-like masses of tissue which contains giant cells, a condition to which the term epulis has been applied (Fig. 317). This lesion differs from that above described in that the former arises from the periosteal or subperiosteal tissue rather than within the bone. The matrix is usually quite dense and fibrous, and the condition gives the impression of a benign, chronic inflammatory process with foreign body giant cells. Kittel[33] has described a giant-cell tumor of the upper jaw of a boy aged 5½ years under the designation of myeloma. Lewis,[34] who described a "giant-cell tumor" of the dorsal vertebræ of a girl aged seven years, apparently cured 2¾ years after operative removal and radiation treatment, was able to collect from the literature 16 examples of this lesion involving the vertebral column. Five of these occurred in children, the age and sex being as follows: Two girls aged 13 years; one boy aged 14 years; and two males aged 16 years. Of this group of lesions in children all were successfully operated upon except one.

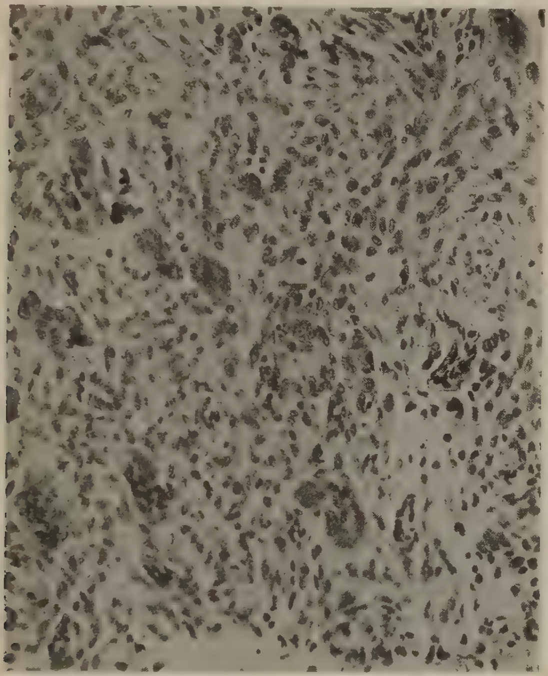

FIG. 317.—Epulis of jaw; male infant aged 17 months. ×230.

Alveolar Sarcoma.—Of sarcomas which have received special names because of the arrangement of their cells, the alveolar sarcoma is so termed because the tumor cells arrange themselves in solid nests or alveoli of variable size, which are separated from each other by stroma. An alveolar arrangement is so characteristic a feature of lepidic tumors that one is inclined to view with skepticism the belief that alveolar sarcomas are merely sarcomas of indifferent supporting tissue. The burden of proof that such sarcomas are not medullary carcinomas or endotheliomas rests upon the observer who uses the term alveolar sarcoma.

Cautley[35] reported an alveolar sarcoma with multiple metastases of the skull and superficial lymph nodes, in a child aged 2½ years. There were large tumor masses in the iliac fossæ. The tumor tissue had a greenish tinge, but the blood picture was not that of chloroma. It is impossible to determine what the exact nature of this neoplasm may have been, but the description suggests the aleukemic form of chloroma. Boschowsky's[6] collection of primary sarcomas of the lung includes an alveolar medullary sarcoma of the right upper lobe in a boy aged 10½ years. In a tabulation of 178 cases of primary sarcoma of the pelvic bones, made by Schmidseder[36] in 1914, there is an alveolar sarcoma of the sacrum, with involvement of the pelvic organs, in a child 1¾ years old; it is probable that this was a sacrococcygeal mixed tumor. Wolff[37], who recognized the morphologic similarity of alveolar sarcoma to endothelioma and carcinoma, but believed that the former could be differentiated, found 14 sarcomas of the ovary in the material of the Heidelberg Frauenklinik during a period of 10 years. Four of these tumors he termed alveolar sarcoma; two of these were large tumors in girls aged respectively 15 and 16 years.

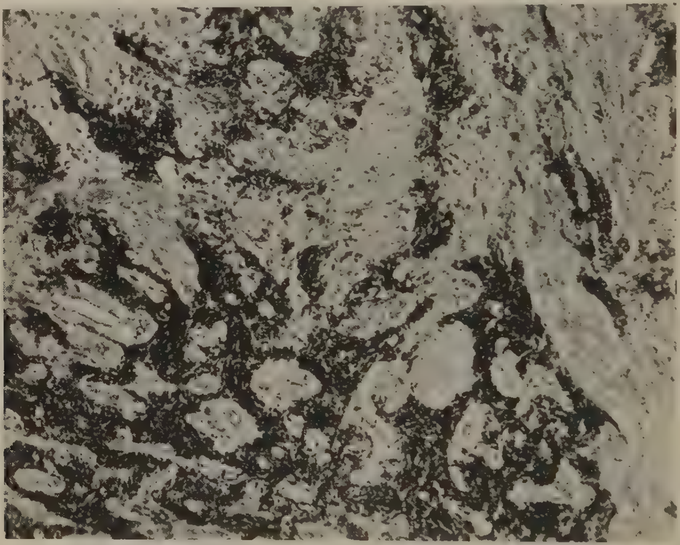

FIG. 318.—Perivascular sarcoma of scapula; girl aged 10 years. ×90.

Perithelial Hemangiosarcoma.—Certain hylic tumors are characterized by the presence of numerous blood-vessels, about which the tumor cells form thick, prominent, cellular mantles (Fig. 318). In certain instances such a peculiarity of arrangement is undoubtedly due to necrosis of tumor tissue, with preservation of that immediately about the vessels. Concerning the nature of those neoplasms in which simple necrosis is not an adequate explanation of the features observed, no very definite conception exists in the textbooks of pathology. Apparently tumors of diverse origin are included in the perivascular sarcoma group. If this term is to be used for neoplasms derived from ordinary supporting tissue, it should be applied to those in which the tumor cells arise from the adventitial connective tissue elements of the vessels, growth of the latter going hand in hand with the adventitial proliferation.

Very few of the described perivascular sarcomas have such an origin or mode of growth. Most of them, and this is especially true of those which have been reported in children in the choroid plexus by Wätzold[38] and by Besold (Merkel[4]), in the pineal body by Goldzieher,[39] and in the coccygeal gland by Buzzi,[40] appear to be endothelial or paraganglionic in origin, and therefore endothelioblastomas or paragangliomas, and not simple sarcomas. Borrmann,[41] in a discussion of the nomenclature of the vascular tumors, divided them into the following groups: (1) Angioma, which includes the cavernous hem- and lymph-angiomas already discussed above under the benign tumors. (2) Angio-endothelioma, subdivided into hemangio- and lymphangio- endothelioma. (3) Perithelioma. (4) Peri-endothelioma. If there actually occurs a perivascular sarcoma due to proliferation of adventitial tissue rather than endothelium, it would belong in Borrmann's third group of perithelioma, a name unfortunately applied by a number of writers to tumors derived from perivascular lymphendothelium, i.e., the peri-endothelioma group of Borrmann, and by others to tumors of organs in which the parenchymatous elements lie directly upon the walls of capillary vessels, as in the adrenal cortex and the carotid body.

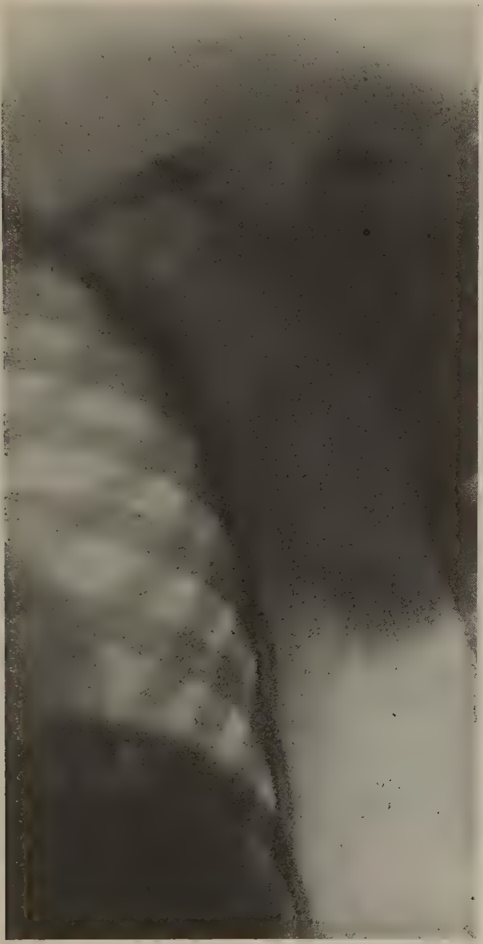

FIG. 319.—Roentgenogram of perivascular sarcoma of scapula before treatment.

Myxosarcoma.—Chondrosarcoma.—Osteosarcoma.—These terms are applied to sarcomas which contain respectively mucoid, cartilaginous or osseous tissue.

Frequently a sarcoma may contain the three kinds of tissue. The usage of the terms is rather inexact in the literature, being applied on the one hand to neoplasms which contain mucoid tissue because of degenerative changes or bone and cartilage because an ordinary sarcoma has invaded these tissues; and on the other hand, they are applied to tumors composed of cells which have the specific property of forming bone or cartilage. If we are to attempt a subclassification of sarcoma, those tumors made up of chondrogenic or osteogenic tissue should be placed with the malignant hylic tumors of specific tissues. Sarcomas of children frequently contain mucoid tissue. Usually this appears to be the result of edema and of degenerative changes in the non-specific sarcomatous matrix. In some of the congenital sarcomas the mucoid tissue is embryonic tissue which contains true mucin. Three myxosarcomas of the bladder in children are included in Wilder's[17] collection of cases. Tumors of the vagina in children may be of myxosarcomatous character. McFarland's[21] table contains two such tumors. Many of the bone and cartilage containing tumors of children, especially those which arise in situations which normally do not contain bone or cartilage, are mixed tumors or teratomas. Raoult[42] recorded an inoperable, recurrent sarcoma of the nose of a girl aged 15 years; a tumor which had obstructed the left naris and which was termed an osteosarcoma had been removed when the child was nine years old.

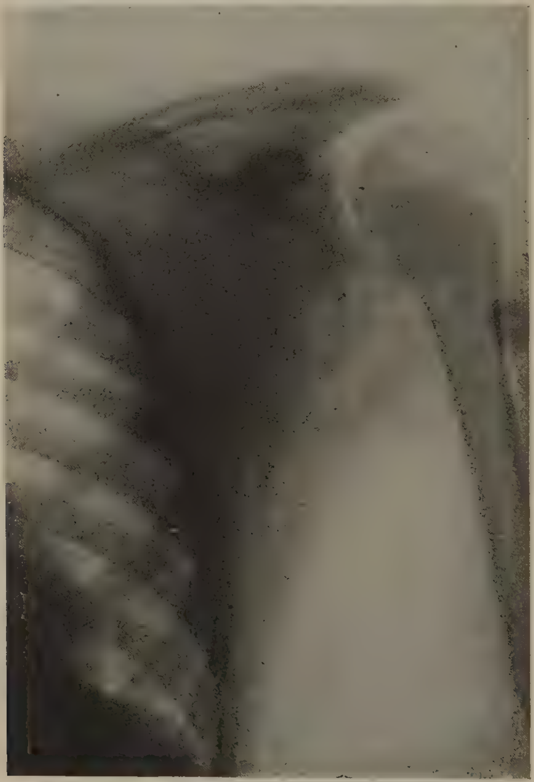

FIG. 320.—Roentgenogram of perivascular sarcoma of scapula after short wave-length roentgen-ray therapy.

MALIGNANT HYLIC BLASTOMAS OF SPECIALIZED MESOBLASTIC TISSUES

Myxoblastoma.—The neoplasm termed myxosarcoma is usually a soft fibroma whose mucoid character is the result of edema and degeneration. A few tumors composed of embryonic mucoid tissue, whose cells, like those of Wharton's jelly, have the property of forming a mucinous ground substance, have been reported as arising from the umbilical cord or umbilicus. Kaufmann[43] reported such a myxosarcoma of the umbilicus, which was present at birth and grew progressively; it was covered in part by skin and in part by amnion, and contained numerous wide, cavernous blood-vessels. Cullen[44] includes two other congenital umbilical tumors of this type.

Lipoblastoma.—Tumors composed of young cells of the type which make up embryonic adipose tissue are rare. Groups of such cells are sometimes seen in lipomas which otherwise are benign and in which the young cells show no tendency to invasiveness. It is possible that some of the neoplasms described as xanthomas may be lipoblastomas, rather than fibromatous tumors or granulomas whose cells have become secondarily infiltrated by lipoid material (Fig. 321).

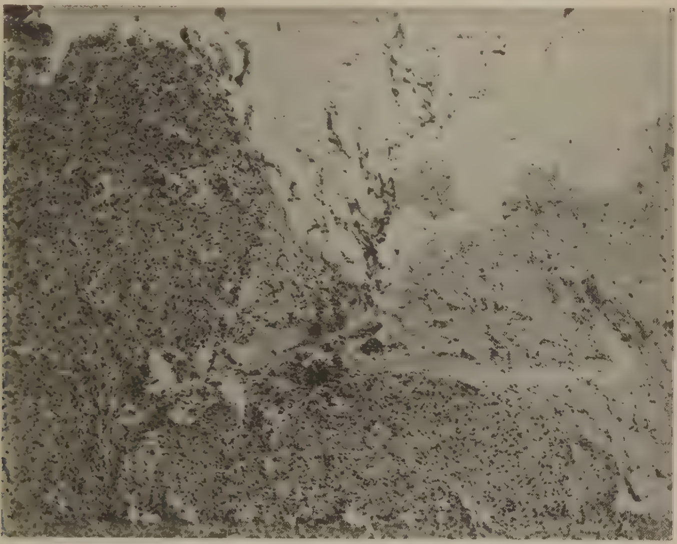

FIG. 321.—Lipoblastoma of subcutaneous tissue; girl aged 9 years. ×80.

Fibroblastoma or Spindle-cell Sarcoma.—The spindle-cell sarcoma is as widespread in its origin and distribution and perhaps is as frequent in its occurrence in children as the round-cell sarcoma. Its name is derived from the fact that it is composed of spindle shaped cells, which are longer than they are broad. The cells may vary in length and in breadth; the shorter forms, occurring in the more cellular tumors, are often referred to as "oat shaped." The cells are usually arranged in bundles of variable size, which run in various directions through the tissue. By proper staining methods after suitable fixation, the presence of intracellular fibroglia fibrils can be detected even in the younger cells; as the cells become larger, varying amounts of intercellular fibrillar ground substance are formed. The formation of fibrils is, of course, an evidence of some degree of differentiation of the tumor cells, and clinically as well as microscopically the spindle-cell sarcoma is less malignant than the round-cell form. Since the neoplasm is composed of connective tissue cells which have the property of forming fibrils characteristic of such cells, it might properly be termed a fibroblastoma to indicate the origin of its cells.

Spindle-cell sarcoma arising from the periosteum is probably the most frequent form of tumor of the skeleton in children. An interesting example of such a tumor is the spindle-cell sarcoma of the humerus presented by Sherwood[45] before the New York Surgical Society in 1923; the tumor was present at birth and within three weeks had extended from the shoulder to the elbow. Rocher[46] reported a spindle-cell sarcoma of the spinal column, periosteal in origin, in a child 13 months old. In addition to the periosteum, the subcutaneous tissue and the intermuscular fasciæ are frequent sites of spindle-cell sarcoma. A vascular spindle-cell sarcoma of the neck was reported by Gaifami;[47] the tumor was present at birth in a premature infant and had led to metastases in utero. Keenan's[5] group of sarcomas of the tongue included three spindle-cell tumors, in children aged respectively 11 weeks, 4 years, and 17 years. Boschowsky's[6] tabulation of primary sarcomas of the lung contains a spindle-cell sarcoma of the right upper lobe, 10 cm. in diameter, in a girl aged 14 years. Fetzer (in Mönckeberg[9]) reported a spindle-cell sarcoma which measured 16 by 9 by 18 cm. and filled almost the entire thorax of a child; it was believed to have arisen from the mediastinal connective tissue. A spindle-cell sarcoma of the pleura which filled the right thorax of a girl aged 15 years, recorded by v. Dieballa and Entz,[48] was associated with bone metastases and a leukemic blood picture. Hutchinson[49] many years ago reported a "fibrocellular tumor" of the prepuce of the penis of a boy aged eight years; since the lesion had not recurred within five months after its local and incomplete excision, some doubt may be expressed as to its neoplastic nature.

In view of the rarity of spindle-cell sarcoma of the intestine, Telling's[50] case of such a tumor of the small intestine of a boy aged 3½ years is of interest. Demel[51] has described a large, pedunculated, partly degenerated and cystic spindle-cell sarcoma of the stomach of a girl eight years old. Gosset, Bertrand and Loewy[52] have recently expressed a doubt concerning the nature of the pedunculated tumors of the stomach usually termed sarcomas or myosarcomas. They believed that these tumors are derived from sheath of Schwann cells and proposed the name "schwannoma;" if their view is correct, the name neurinoma, already applied to cellular tumors originating from the neural sheath cells, would be preferable. Their collection of such tumors included two in girls aged 17 years. The successful removal of a fibrosarcoma of the posterior surface of the cauda equina, which had first produced symptoms when the patient was 10 years old, was reported by Elsworth.[53] Jepson and Albert[54] described a fibrosarcoma which was present in the spleen removed surgically from a girl aged 15 years; the tumor was encapsulated and measured 9.5 by 8.2 by 7.7 cm. The patient was in good health 10 months after the splenectomy. Among the 15 primary sarcomas of the bladder in children included in Wilder's[17] tabulation of 50 cases, were 3 examples of spindle-cell sarcoma in boys aged respectively 1¾, 5 and 8 years. Five spindle-cell sarcomas of the prostate appear in Sysak's[18] group of 22 prostatic tumors of childhood. The 23 cases of sarcoma of the thymus in children which Rubaschow[15] collected included one spindle-cell sarcoma. A spindle-cell sarcoma of the ciliary body, in a man aged 20 years in whom the tumor had been present for 12 years, is included in Li's[55] collection of the rare ring sarcomas of the eye. Obendorfer[56] saw a spindle-cell sarcoma of the subcutaneous tissue which followed a subcutaneous injection.

Myoblastoma.—Malignant tumors composed of or containing immature and partly differentiated muscle may arise from smooth muscle, leiomyoblastoma, or from striated muscle, rhabdomyoblastoma. In the adult such a malignant transformation sometimes occurs in the fibromyomas of the uterus and of the gastro-intestinal tract, the resulting tumor being characterized by the presence of multinucleated giant cells of smooth muscle origin intermingled with young spindle cells. According to Merkel,[4] the occurrence of leiomyoblastoma in childhood had not been noted up to the date of his publication (1912), and we have been able to find no certain case since that time. The rhabdomyoblastoma is one of the neoplasms peculiar to the early years of life and has already been sufficiently discussed above.

Chondroblastoma.—Osteoblastoma.—With these terms we may designate neoplasms made up of immature cartilage or bone forming cells, in contradistinction to chondrosarcoma and osteosarcoma, ordinary sarcomas which have invaded cartilage or bone. Tumors whose cells have the property of forming the last named tissues arise usually in connection with the skeleton, that is, from pre-existing bone and cartilage and their membranes, more rarely from misplaced or heterologous bone and cartilage. The latter tissues are frequent constituents of mixed tumors, cartilage especially being a prominent element in the mixed salivary gland tumors, in the mixed tumors of the kidney and vagina, and in more complex teratomas. These are not to be included among the chondroblastomas and osteoblastomas. In the latter, cartilage and bone often occur together in the same tumor, the differentiation of formative cells into cartilage and bone following along normal lines in different areas of the tumor. In osteoblastomas without cartilage, sometimes termed osteogenetic sarcomas or osteoidsarcomas, areas of cellular, undifferentiated tissue alternate with others made up of uncalcified osteoid tissue and with trabeculæ of bone covered with one or more layers of osteoblasts (Fig. 322). Osteogenesis leads to the formation of irregular masses and projections of osseous tissue and to deformity of the involved bone. Local metastasis may lead to the formation of masses of bone in the surrounding soft tissues which have no direct connection with the bone of the original tumor. In children the scapula, ribs, skull and pelvis are more often the site of bone and cartilage forming neoplasms than the long bones. The osteoblastoma may decrease in size rapidly under short wave-length roentgen-ray therapy; the differentiated, new formed bone does not, of course, disappear.

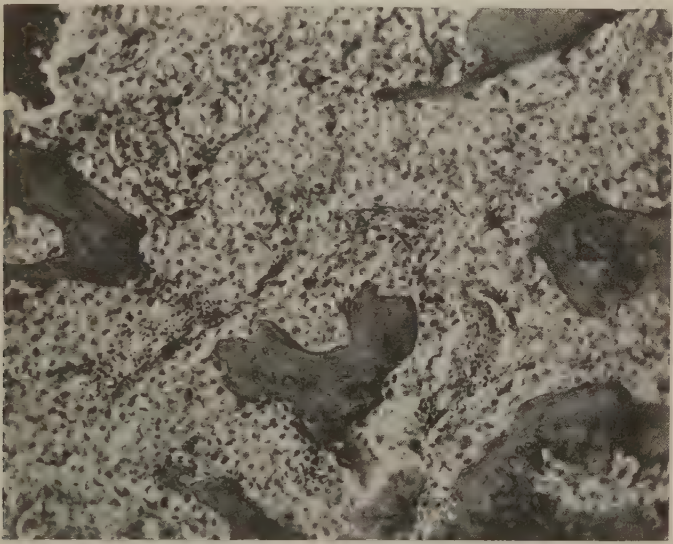

FIG. 322.—Osteogenic sarcoma of skull; boy aged 15 years. ×140.

Melanoblastoma.—Although the eye and the pigmented mole of the skin not infrequently give rise to highly malignant tumors in the adult, such tumors are extremely rare in children. Li,[55] who reported a melanoblastoma of the iris of ring form in a young man aged 22 years, was able to find only five previously reported examples of sarcoma of the iris. One of these, a melanoblastoma in a girl aged 12 years, was associated with a pigmented nevus which had been present at the lower outer quadrant of the eye for several years and which had recently increased in size. Netherton[59] has described as a melanoma a tumor of a girl aged two years which began as a small lump in the lower lip at the age of six months, increased rapidly in size, involved both lips, and metastasized to the lymph-nodes of the neck. Although the tissue removed from the original tumor contained no pigment, the metastases were considered characteristic. Cullen[44] credits to Volkmann a cherry-sized melanotic sarcoma of the umbilicus in a young girl; wide removal of the tumor was followed by recurrence, metastasis and death. Reinmann[58] reported a pigmented tumor which involved both adrenals of a three months old infant and led to widespread metastasis throughout the body. He termed the neoplasm a melanotic carcinoma; it appears more probable that the tumor was an adrenal phæochromoblastoma.

Lymphoblastoma.—Tumors made up of round cells of lymphocyte type and termed lymphosarcomas (lymphoblastomas) are among the most frequent form of malignant hylic tumor in childhood. No sharp distinction is made in the literature between round-cell sarcoma and lymphosarcoma, and it is impossible to make a distinction in many cases from the morphology of the tumor tissue. The origin of a neoplasm in lymphoid tissue and its metastasis to other lymph nodes are presumptive evidence that the tumor is lymphadenoid in origin. But upon theoretical grounds we must admit the possibility of the derivation of round-cell tumors from the supporting elements of lymphoid tissue, and conversely, because of the frequency with which lymphoid tissue may develop in tissues in which it does not usually occur, we must grant the possibility of the origin of lymphoblastomas in organs usually free of lymphoid tissue. The question is largely an academic one, since the round-cell sarcoma derived presumably from immature supporting tissue and the lymphosarcoma are so similar clinically and morphologically. A differential point which sometimes is helpful in distinguishing the two is the more marked tendency of the cellular sarcoma originating in lymphoid tissue, and presumably a lymphoblastoma, to form narrow cords one or two cells wide, separated from each other by strands of reticulum, an arrangement which one frequently sees in the peripheral zone of normal lymph-nodes. The lymphoblastoma may be composed of cells whose diameter approximates that of the small lymphocyte, or of larger cells more like the large lymphocyte. The small celled is the more frequent variety.

The lymphoblastomas of children arise most often from the retroperitoneal, mesenteric and mediastinal lymph-nodes, and more rarely from the cervical and superficial nodes. In the mediastinum it is often impossible to determine whether the tumor had its origin in the thymus or in the lymph-nodes. Rosenson[59] found 15 of 38 mediastinal tumors of children listed as sarcoma and believed that most of these were lymphosarcomas which had arisen from the thymus. Peters,[60] in 13 cases of primary sarcoma of the mediastinum and lungs encountered at the Montreal General Hospital in the four years from 1920 to 1923 inclusive, had one case of round-cell sarcoma in an eight year old boy, which filled the left pleural cavity and had completely replaced the left lung. The exact origin could not be determined, but the mass arose presumably from the hilus nodes of the left side. L'Huillier[61] reported a lymphosarcoma of the head of the pancreas of a female infant which died at the age of nine days of an umbilical infection. In three previously reported cases in children, in whom the pancreatic tumor was part of a more widespread involvement by lymphosarcoma, this writer believed the pancreas to have been secondarily involved. Rabé and Denis[62] described a round-cell sarcoma, probably a lymphoblastoma, of the tonsil in a boy aged nine years. Mönckeberg[9] gives the following tumors of the intestine in children: A case reported by Robertson and Given, in a child of five years; the tumor measured 15 cm. in diameter and was said to have arisen in the submucosa of the jejunum. A small round-cell sarcoma of the size of the fist, situated 2 m. above the ileocecal valve; the tumor was reported by Hiost in a boy aged seven years. A lymphosarcoma of the ileocecal region in a boy aged 11 years, credited to Reuterskiold.

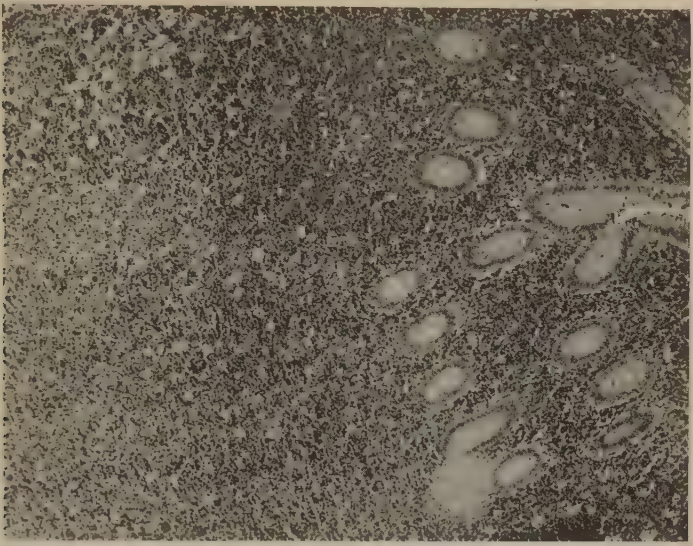
Fig. 323.—Lymphoblastoma of appendix; girl aged 9½ years. Diffuse involvement of mucosa.

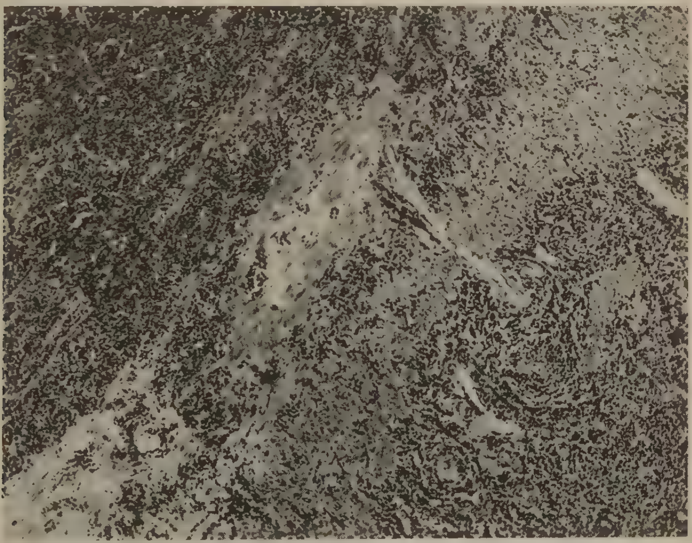
Fig. 324.—Lymphoblastoma of appendix. Invasion of muscle coats and serosa. ×90.

Corner and Fairbanks[63] described as "adenoma-like" a tumor removed from the colon of a boy aged nine years; three months later a small round-cell sarcoma was found in the same situation and at this time the lymph nodes were involved. Mirotworzew and Sacharow's[64] compilation of 31 cases of primary sarcoma of the intestine included four in children; one of these was a round-cell sarcoma, probably lymphoblastoma, of the small intestine of a boy aged six years. Hünermann,[65] in a study of benign and malignant non-carcinomatous neoplasms of the stomach, reported a lymphosarcoma of the pyloric region of the stomach of a child aged six years. We have recently seen a lymphoblastoma of the appendix, in a girl aged 9½ years (Figs. 323 and 324). Removal of the appendix was followed by recurrence, metastasis and death.

The lymphoblastomas noted above are of the kind which begin in the lymphoid tissues at some local point, and spread rapidly by local invasion and by metastasis by both the lymph and blood channels. In children there occur also malignant hyperplasias, the lymphosarcomatosis of Kundrat[66] and Paltauf,[67] which involve the lymphoid system so widely as to suggest a blastomatous system affection rather than a local tumor which has spread by metastasis.

Myeloblastoma.—Tumors derived from the specific bone marrow cells may be termed myeloblastomas. The bone marrow of post-fetal life contains two kinds of cells which may be considered specific, myeloblasts and erythroblasts, whose functions are the formation respectively of leukocytes and erythrocytes. This statement is made without prejudice in regard to the unitarian, dualistic or polyphyletic doctrines of the origin of the blood cells. It is meant to indicate only that when cellular differentiation in the bone marrow has proceeded to such a degree that recognition of cell type is possible, the two types mentioned must be considered specific marrow elements in that they do not occur normally elsewhere, whereas the other cellular constituents of the marrow may and do occur in other situations. It should be theoretically possible, therefore, for two types of specific bone marrow cell neoplasms to occur, myeloblastoma in the stricter sense, composed of young cells of the leukocytic series, and erythroblastoma, composed of young cells of the erythrocytic series. But the marrow contains also formative cells of the lymphocytic series. These may and do give rise to lymphoblastomas of the kind described above, that is, localized, primary lymphoblastomas which invade and metastasize.

Multiple Myeloma.—There may occur also in the skeletal system tumors composed of cells apparently of the lymphoid type, such tumors differing clinically from the usual form of lymphoblastoma and being referred to usually as multiple myelomas. Frequently this form of tumor is composed of cells morphologically like plasma cells and for this variety the name plasmacytoma has been proposed. In view of the still unsettled origin of the plasma cells of non-neoplastic conditions, and of the controversy as to whether this cell belongs to the lymphocytic or myelocytic series, or is a derivative of the reticulo-endothelial system or of ordinary connective tissue, it is not surprising that there should be discussion as to whether the plasma cell myeloma is a lymphoblastic myeloma, a myeloblastic myeloma, or a tumor which is not derived from cells of the hematopoietic system. Clinically the tumor, occurring usually in adult life, is characterized by its multiple involvement of the skeletal system and by its slow and relatively benign course. Occasionally the plasma cell myeloma is locally invasive, and Kreibich[68] has described such a tumor in an adult, which was associated with invasive, tumor-like nodules of plasma cells in the skin. Ghon and Roman,[69] and Hertz and Mamrot[70] have reported cases, also in adults, in which there was widespread hyperplasia of the lymphoid tissues due to plasma cells. The lymphocytic multiple myelomas are in general like the plasmacytic forms, but show a somewhat greater tendency to local invasiveness. Direct transition of lymphocytes to plasma cells in some myelomas is evidence of the close relationship of the two forms of myeloma. The occurrence of Bence-Jones proteinuria and the antigenically specific character of this protein, as shown by Hektoen[71] and by Everett, Bayne-Jones and Wilson,[72] may be mentioned, if only to call attention to the fact that the excretion of Bence-Jones protein is not limited to multiple myeloma.

The multiple myeloma is a tumor of adults and is usually of the plasma cell or lymphocytic type. de Elizalde and Llambias,[73] however, in 1914 reported a multiple myeloma of a child aged five years. The tumors, which were present in the skull and vertebræ, were composed of plasma cells, with which a few lymphocytes were intermingled. There have been reported in children a few examples of multiple marrow tumors composed of myeloblastic cells. These neoplasms have been highly malignant. Roman[74] reported two such cases in 1912, one in a girl aged two years and one in a boy aged three years. In each case there were multiple tumors of the entire skeleton, including the skull. Most of the nodules were medullary, but some were periosteal. In the second case the clinical diagnosis was chloroma, but in neither instance was there any change in the circulating blood except a secondary anemia. Metastases were present in the lymph-nodes, and in the second case in the liver. The tumors were composed of young, undifferentiated cells like myeloblasts and of other cells which had the characteristic granules and morphology of myelocytes. Roman believed these tumors to be multiple primary neoplasms of the bone marrow and proposed the name myeloplastic sarcoma for them. He could find in the literature four other cases of multiple bone tumors in children. Marchand's pathologic diagnosis in one of these, which occurred in a girl nine years old, was primary myelogenous sarcoma of the skull. In the other three cases, recorded respectively by Gussenbauer and Chiari in a 17 year old boy, by Dittrich in a 2½ year old boy, and by Schmidt in a 2 year old boy, the tumor cells did not have the characteristics of myelocytes, and Schmidt considered them examples of pseudoleukemia. Berkheiser,[75] in 1924, reported two additional cases of multiple myelomas in children. The first of these was a boy aged 12 years, with tumors of most of the vertebræ and ribs, of the right scapula, the skull, the pelvis and the bones of the extremities. They were composed of cells of the type of myelocytes, with which a few plasma cells were intermingled. In the second case, a girl aged 3½ years, there were multiple tumors of the pelvic bones, femur, humerus, and skull. The tumor tissue was made up of elongated, often foamy cells, believed by Maximow to be reticular in origin, and of myelocytes.

Erythroblastoma.—The theoretical possibility of occurrence of a neoplasm composed of primitive erythroblasts, an erythroblastoma, has been mentioned above. This tumor is a pathologic curiosity, the only reported case being that of Ribbert;[67] this was an adult.

The relative frequency of the various forms of myeloma is apparent from the critical review published by Hirschfeld,[77] who analyzed 93 cases published previous to 1910; all were adults. Fifty-one of these were from the older literature, with histologic descriptions inadequate for a determination of the cell type. Three examples of multiple bone tumors were excluded by Hirschfeld because he believed that the histologic study showed that they were not myelomas. The remaining 39 multiple myelomas were classified according to cell type as follows: Lymphocytic, 12; myelocytic, 13; plasmacytic, 13; erythroblastic, 1. The greater preponderance of such neoplasms in adults is also illustrated by Martiri's[78] tabulation of 204 cases reported prior to 1915, all of which were in adults. He omitted, however, the two previously published cases of Roman, which were apparently true myeloblastomas, and the case of de Elizalde and Llambias.

Leukemia.—The leukemias present many aspects of similarity to neoplastic disease and may receive brief consideration at this point, in connection with the other tumor-liked hyperplasias of the lymphoid and myeloid tissues. Whether leukemia is actually a blastomatous condition is still a matter for controversy, into the details of which we need not enter. The arguments for and against have been sufficiently set forth in the publications of v. Domarus,[79] Herz,[80] Pappenheim,[81] Naegeli[82] and others and in the various text-books of pathology. The many resemblances which the acute forms bear to infectious processes have been recently reviewed by Catsaras;[83] it may perhaps ultimately become possible to make a sharp distinction between the acute and chronic forms of leukemia. The progressively downward clinical course of the latter and the cellular infiltrative changes in the internal organs suggest a blastomatous process; the absence of evidences of local invasion are contrary to our usual conception of malignant neoplasms. The clinical manifestations of leukemia have been taken up in a previous volume (Lucas; Chapter LXXVII, Vol. IV). At this point we shall consider the leukemias of children only from the standpoint of their similarity to the lymphoblastomas and the myeloblastomas already discussed and to certain other abnormalities of the hematopoietic system which still remain for discussion.

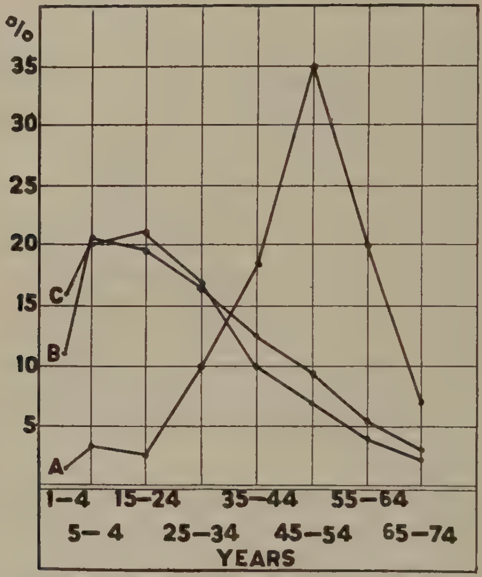

Chart 4.—Age incidence of lymphatic leukemia. (Minot and Isaacs.[84]) A, Percentage age distribution of population (U. S. and British). B, Percentage age distribution of chronic lymphatic leukemia (based on 84 cases of Ward and 92 cases of Minot and Isaacs). C, Percentage age distribution of acute leukemia (based on 398 cases of Ward and 57 cases of Minot and Isaacs).

Lymphoid Leukemia.—This is the more frequent form of leukemia in children, in whom the disease usually runs a more rapid course than in adults. The age incidence of lymphatic leukemia has been recently determined by Minot and Isaacs[84] upon the basis of 98 cases of the chronic form and 57 cases of the acute form, personally studied by the authors, and by Ward[85] in 84 British cases of chronic lymphoid leukemia and 398 cases of acute leukemia. In the last group no distinction was made between the lymphoid and myeloid forms; since acute myelogenous leukemia is rare in childhood, Ward's figures may be applied to the acute lymphoid types (Chart 4). In 176 cases of chronic lymphatic leukemia the ratio of males to females was three to one; in 57 acute cases it was four to one. In the very young, the proportion of females is somewhat higher.

Lymphoid leukemia is characterized anatomically by hyperplasia of the lymphoid tissue and only moderate enlargement of the spleen; similar hyperplasia may also be present in the bone marrow. In its earlier stages the process appears to be a pure hyperplasia, which is not to be differentiated microscopically

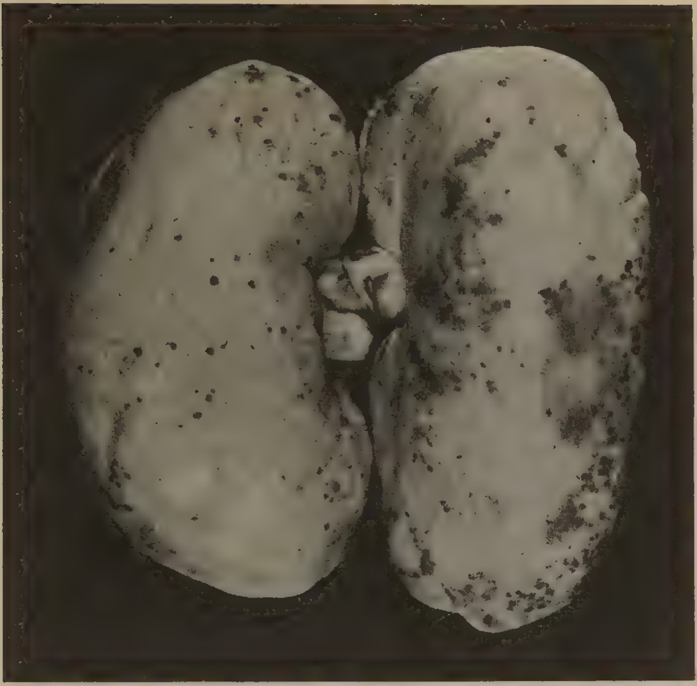

Fig. 325.—Enlargement of kidneys due to leukemic infiltration, with multiple hemorrhages; boy aged 4 years.

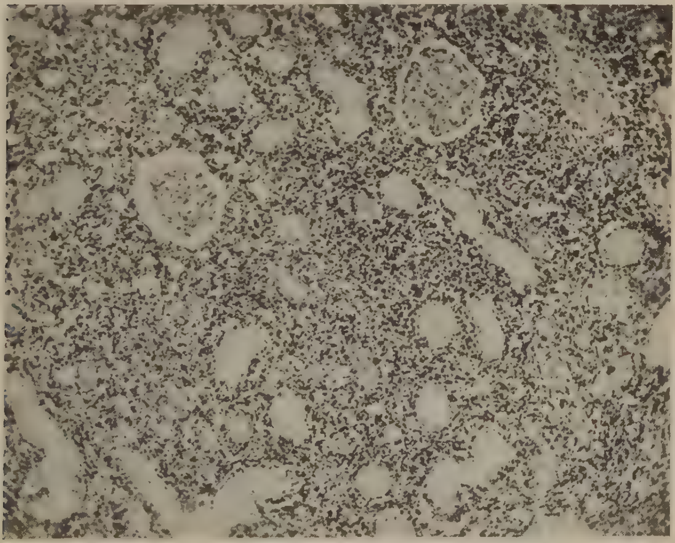

Fig. 326.—Leukemic infiltration of kidney. ×140.

from the benign hyperplasias or lymphomas. The follicular arrangement of the lymph nodes may be preserved at this stage, the chief change being an increase in the size of the germinal centers of the follicles and an increase in the width of the peripheral zone of small lymphocytes. Later the normal follicular architecture disappears and the entire node is diffusely hyperplastic. In typical cases there is little or no local invasion, the lymph-nodes remain unfused, and the enlargement is only moderate. The internal organs are the seat of lymphocytic infiltration of varying degree; in some cases this may be so extreme that the parenchymatous elements are hidden by the infiltrating cells (Figs. 325 and 326). Leukemic nodules occur in the skin; rarely the infiltration of the skin may be so diffuse as to suggest sarcoma cutis. In the acute cases hyperplasia of the intestinal lymphoid tissues may be associated with necrosis, ulceration and hemorrhage. Sérard[86] reported two cases of acute lymphoid leukemia, in a girl aged five years and a boy aged 16 years, with marked enlargement of the thymus, which weighed respectively 150 and 60 gm. Rocaz[87] recorded a similar case in a child of four years, in whom the thymus measured 12 by 10 by 4 cm. and weighed 200 gm.

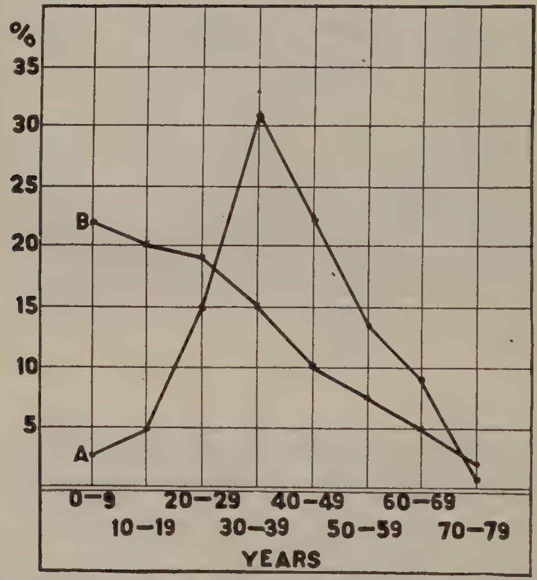

CHART 5.—Age incidence of myeloid leukemia. (Minot, Buckman and Isaacs.[88]) A, Percentage age distribution of population (U. S., 1910). B, Percentage age distribution of myeloid leukemia (based on 166 cases of Minot, Buckman and Isaacs).

Myeloid Leukemia.—This is a relatively rare condition in childhood. In Minot, Buckman and Isaacs'[88] series of 166 cases, there were only eight cases under 20 years of age (Chart 5). The sex distribution is more nearly equal than is true of the lymphoid form; in a total compilation of 605 cases, 60 per cent. were males and 40 per cent. females. Below 25 years of age the proportion of females was somewhat higher. In the very young the condition is so rare that several writers have claimed that the few reported cases are not true leukemia, but examples of pseudoleukemia infantum or of infection. Solmitz,[89] who reported a case in a boy aged 1½ years, could find only three reported cases under four years of age which he was willing to accept as true leukemia. Isaac and Cobliner[90] reported two cases, one in a girl aged 18½ months and one in a boy aged 6 months, which they believed to be microlymphocytic type of acute myeloid leukemia. This conclusion was based upon the myeloid hyperplasia of the hematopoietic tissue, whereas the hematologic picture was characterized by the presence of 72 and 82 per cent. of small lymphocytes respectively. The authors believed that the circulating cells were not true lymphocytes, but atypical myeloblasts.

In myeloid leukemia enlargement of the spleen and hyperplasia of the bone marrow are more marked than in the lymphoid variety, and the lymph-nodes are enlarged to a lesser degree. Histologically the process is one of myelocytic hyperplasia of bone marrow, and of myeloid transformation of the spleen and lymph nodes. The internal organs are infiltrated by myelocytes and myeloblasts. Whether the myelocytic cells present elsewhere than in the marrow are the result of infiltration by cells derived from the marrow or have been formed locally by myeloid transformation of indifferent stem cells is still a matter for argument. Rautmann[91] is one of the most recent to describe the transformation of the endothelium of capillaries into myelocytes.

Mixed Leukemia.—That there is such a condition as mixed leukemia has been denied by many, if not most writers. Thus Herxheimer,[92] who maintained a strictly dualistic viewpoint, insisted that the transformation of one form of leukemia into another did not occur and that there could be no dedifferentiation to a stem cell stage which would give rise to both myeloid and lymphoid elements. Isaac and Coblinear[90] said that their two cases might perhaps be considered mixed leukemia, but they themselves did not accept such a possibility. Logefeil[93] has recently made a study, under the direction of the hematologist Downey, of a case in a six year old girl, which he believed to be a true mixed leukemia. His conclusion was based upon the presence in the circulating blood of cells believed to be indifferent stem cells, of lymphocytes and lymphoblasts, and of myelocytes and myeloblasts, and in the hematopoietic tissues of lymphoid hyperplasia and myeloid transformation side by side. The condition was interpreted as one in which proliferation of indifferent stem cells had given rise to cells of both the lymphocytic and myelocytic series. He analyzed the previously reported cases of mixed leukemia.

Leukosarcomatosis.—Sternberg,[94] in 1904, upon the basis of histopathologic study attempted to separate from the group of cases with the hematologic picture of lymphoid leukemia certain cases to which he applied the name leukosarcomatosis. Cases of this type were characterized by the presence in the blood of large mononucleated cells, which he believed to be young, unripe lymphocytes or lymphoblasts. Anatomically the condition differed from the typical lymphoid leukemias in a more marked invasiveness of the hyperplastic lymphoid tissues, usually most marked in the mediastinal lymphoid apparatus. The invasive properties of the tissue Sternberg believed to be evidence of a true blastomatous condition, as opposed to the more purely hyperplastic process which he believed to be the essential condition in the leukemias.

Although opposed by Graetz,[95] Herxheimer,[92] Fraenkel,[96] Pappenheim[81] and many others, Sternberg[97] continued to maintain his position, summarizing his views in 1916 upon the basis of 8 cases which he believed to be leukosarcomatosis and 21 which he admitted were myeloblastic leukemia. He had by this time altered his original viewpoint sufficiently to admit that the large mononuclear cells, which he had first thought to come from lymphoid tissues, were myeloblastic in some cases. Those who have opposed him believe that among the hyperplastic diseases of the hematopoietic system there occur all gradations from benign hyperplastic conditions without blood changes to highly invasive and clinically and anatomically malignant processes with or without leukemic blood changes, and that it is improper, therefore, to set aside leukosarcomatosis as a sarcomatous leukemic entity distinct from the usual form of lymphoid leukemia. Most observers have also disagreed with Sternberg's original view that the large mononuclear cells present in the blood in so-called leukosarcomatosis are lymphocytes. They hold that they are myeloblasts, or perhaps indifferent stem cells, and that Sternberg's leukosarcomatosis is more closely related to myeloid leukemia than to the lymphoid form.

Chloroma.—Described first as a primary periosteal sarcoma of the cranial bones characterized by an evansescent green color, chloroma became the subject of discussion and debate as varied as that which relates to leukemia. An increasing number of reported cases with pathologic variations removed the condition from the simple local blastomas, in which it had originally been included. Variations in the hematologic picture in cases anatomically characteristic led to doubt as to the propriety of including it among the lymphoid leukemias, where it was next put after Osterwald[98] had described an increase in the circulating large mononuclear cells of the circulating blood in 1881 and the leukemic blood changes had been more carefully studied by Dock[99] in 1893. The controversy is still being waged, with those who look upon the condition as a form of leukemia in the majority at the present time.

Anatomically chloroma shows, in common with leukemia, a diffuse hyperplastic involvement of the hematopoietic system. It differs in its greater invasiveness, simulating in this respect the leukosarcomatosis of Sternberg; in the more frequent involvement of the cranial bones and of the vertebræ, tending to form definite nodules in the former; and in the green color of the tissue. Exophthalmos or deafness are frequent, as the result of involvement of the frontal and temporal bones. The vertebral column may be encased in a layer of greenish, moderately firm tissue, which may also be present within the spinal canal and may surround the cord. The lymph-nodes are enlarged, sometimes only moderately, at other times greatly; the most marked enlargement occurs in the mediastinum, the thymus often participating in children. The spleen is sometimes increased in size, but rarely to the degree that occurs in myeloid leukemia. The lymphoid tissue of the alimentary tract is diffusely hyperplastic; the enlarged solitary follicles and Peyer's patches may ulcerate, and necrosis of the hyperplastic tonsils or pharyngeal lymphadenoid tissue may occur. The liver is enlarged as the result of diffuse infiltration of the interlobular tissue. The kidneys are especially prone to cellular infiltration, either diffuse or nodular. The bone marrow is cellular and hyperplastic, this change being more marked in the spongy bones than in the long ones. In the former, the tendency of the hyperplastic tissue to penetrate the bone by growing along the nerves, blood-vessels and lymphatics leads to the formation of the periosteal nodules and diffuse overgrowths of the skull, sternum and vertebræ, which distinguish chloroma from the usual type of leukemia. The skin is involved less often than in leukemia. Lehndorff[100] described a case in which growth of chloromatous tissue along the bronchi had been associated with greenish sputum during life. Huber[101] reported a case, in a woman aged 21 years, in whom the first detectable involvement occurred in the breast and led to amputation for a supposedly primary mammary tumor; the further course was that of typical chloroma, with green tumors of the skull and lymph-nodes. Trevithick[102] also described a case, a girl aged 13 years, with chloromatous tumors of the mammary glands.

Microscopic study has shown considerable variation in the type of cell concerned in the proliferative process. Most often the hyperplastic tissue is composed of large mononucleated cells with clear cytoplasm and relatively large, vesicular nuclei. It was the morphologic similarity of such cells, present in the circulating blood as well as in the tissues, to lymphoblasts which led to the acceptance of chloroma as a form or variant of lymphoid leukemia. It was, furthermore, this same type of cell, held by Sternberg to be a tumor cell rather than any normal blood cell, which led him[103] and others to consider chloroma a form of leukosarcomatosis. The proliferative activity of the germinal centers of the lymphoid tissues has been held to indicate that such cells do actually belong to the lymphoid series. But the formation of identical cells in the interfollicular tissue and in the bone marrow, and the occurrence of transitional stages to typical granular myelocytes have been considered evidence that some, at least, of the so-called large celled forms of lymphocytic chloroma are myelocytic, or that the undifferentiated cell is a stem cell which can give rise to either lymphocytes or myelocytes. There are cases in which the predominating cell is the typical small lymphocyte, and others in which typical myelocytes predominate. Because of the variations in cell type which have been noted, attempts have been made to subdivide chloroma into small lymphocytic, large lymphocytic, myeloblastic, and myelocytic forms. In some cases of chloroma there is little microscopic evidence of invasion. Most often, however, the hyperplastic tissue can be seen invading the capsule of the lymph-nodes, leading to fusion of the latter and to infiltration of the perilymphadenoid tissues.

Color of Chloroma.—The color, the most striking feature of chloroma, varies from light green to an intense dark green. A peculiarity of the color is its property of fading within a few hours after the removal of the tissue from the body. It can not be made permanent by any known method of preservation of the tissue. Trevithick[104] found that the action of hydrogen peroxide temporarily restored the color to preserved tissues which had been colorless for months. Knowledge concerning the chemical nature of the pigment is very meager. The cells contain fine refractile granules which are soluble in alcohol and ether, and which are stained brown to black by osmic acid. These reactions led Chiari[105] to conclude that the pigment is a lipochrome. Dürck, in discussion of a case presented by v. Bauer,[106] stated that he saw similar granules in the epithelium of the renal tubules; the granules could not be stained by Sudan III. Risel,[107] Gümbel[108] and others believed the pigment to be hematogenous in origin and attempted to identify it with the green hemoverdin, which results when hematoporphyrin is oxidized by nitric acid. Kossel and Giese[109] found that the dried, colorless residue obtained by extracting chloroma tissue first with boiling alcohol and then with ether takes on an intense green color after treatment with ammonium sulphide. They interpreted this as an iron reaction dependent on the presence of free sulphur ions, and looked upon the presence of ionized sulphur in the tissues as the essential factor in the pigmentation of chloroma.

Chloroma is essentially a disease of childhood and early adult life. Lehndorff,[110] in his important monograph of 1910, tabulated 73 cases. Of these, 35 were children 15 years of age or under. Of the 35 children, 21 were males, 11 were females, and the sex of 3 cases was not stated, a preponderance of males over females which holds for leukemia also. The youngest case was a child aged 10 months. Mensi,[111] who reported three cases in 1920, brought the total number of previously reported cases in children up to 14 years of age to 46.

Pseudoleukemia.—Typical leukemia presents distinct hematologic and anatomic characteristics. But so many variations from the typical picture occur that it has become difficult to determine what is and what is not leukemia. On the one hand are conditions with characteristic blood changes, in which a clinical diagnosis of leukemia is the natural and easy one, but the anatomic findings are quite atypical. On the other hand are those conditions with characteristic anatomic changes, but with no hematologic alterations except secondary anemia. For this latter type of disease the name pseudoleukemia was introduced. If this term had been limited to the condition which it was supposed to name, there might be some justification for its use. But it soon became a catch-all for any process in which there was enlargement of the superficial lymph-nodes without an increase in circulating leukocytes. This broadening of the meaning of pseudoleukemia, which was the result of a clinical application of the word without regard to the underlying pathologic changes, has rendered the term such a confusing and meaningless one that many writers have pleaded earnestly that it be dropped completely. A case which is recorded as pseudoleukemia may be any condition in which the physical examination detects enlargement of the lymph-nodes; pathologically and actually it may be an example of generalized benign lymphadenopathy, tuberculosis, lymphogranulomatosis (Hodgkin's disease), lymphosarcoma, or true leukemia in its aleukocythemic stage.

If the term pseudoleukemia is to be retained, it should be reserved only for that condition in which there occurs diffuse, non-invasive hyperplasia of the hematopoietic system without an increase in the number of white cells in the circulating blood. Histologically the hyperplasia may manifest itself as an increase of lymphoid or of myeloid tissue; or it may be due to an increase within the hematopoietic tissues of plasma cells, as in two cases described by Ghon and Roman[69] and the one case reported by Hertz and Mamrot.[70] The latter case was unusual in that the antemortem blood examination gave some hint of the condition present; although the total leukocyte count was normal or subnormal, 5 per cent. of the circulating white cells were plasma cells. Careful observation of certain of the cases of pseudoleukemia over a longer period of time has established the development of a leukemic condition of the blood at some later period; when this happens a so-called pseudoleukemia becomes transformed into a typical leukemia. King[112] found that 5 of 41 cases of lymphoid leukemia and 9 of 64 cases of myeloid leukemia in the Johns Hopkins Hospital series were aleukocythemic at some time. In another group of cases the total leukocyte count may be within normal limits, but the proportion of young lymphocytes or of myelocytes is increased. King included the report of a girl aged 14 years, with a greatly enlarged spleen and moderately enlarged lymph-nodes, in whom the leukocyte count was 7120, with 58 per cent. myelocytes; there was no histologic study of the involved hematopoietic tissues.

Although the blood changes constitute the most striking clinical feature of leukemia, cases in which such changes develop late or those in which there is only a relative increase in the proportion of lymphocytes or myelocytes suggest that the entrance of cells into the blood stream from the hyperplastic tissues is only a secondary and nonessential part of a process, which is characterized primarily by hyperplasia within the hematopoietic system. For this reason certain writers, as Fox and Farley,[113] have proposed that pseudoleukemia be used in an adjectival sense only. The present tendency appears to be to discard the word entirely and to consider those conditions, for which this term might still be used in its strictest application, examples of aleukemic or aleukocythemic leukemia. Many of the reported cases of aleukocythemic leukemia have run an acute clinical course, as in the series recently reported by Baar.[111] Such cases are often suggestive of acute infection, with diffuse proliferative reaction upon the part of the hematopoietic tissues to bacteriemia or toxemia, and in this respect resemble the acute hyperplasias with leukocythemia.

Pseudoleukemic Anemia.—A disease of infancy into whose designation the word pseudoleukemia also enters is the pseudoleukemic anemia of v. Jaksch.[115] Characterized by a blood picture which combines the elements of anemia, in that the erythrocytes are decreased and may show evidences of compensatory erythroblastosis, and of leukemia, in that the leukocytes are moderately increased and may show a relative increase of young lymphocytes and of myelocytes, this disease has been placed in a group for which v. Leube[116] proposed the name leukenemia, connoting either the co-existence of true anemia and true leukemia or the transformation of one into the other. Pseudoleukemic anemia, like pseudoleukemia, has also become a clinical collective term. Pseudoleukemic anemia of infants, according to Pappenheim,[117] is a primary anemia with myeloid metaplasia of the spleen and with intra- and extramedullary erythroblastosis, the myelocytosis being a secondary, reactive phenomenon. Eppinger[118] considers v. Jaksch's anemia the reaction of a functionally inadequate bone marrow to increased blood destruction, the latter being the result of rickets, faulty nutrition, syphilis, etc. In regard to the use of the word pseudoleukemic in the terminology of this condition and any hematologic or anatomic similarity to or relationship with leukemia which it suggests, we may agree with Evans and Happ's[119] conclusion that pseudoleukemic anemia of infants "is not yet entitled to any special name, especially one that suggests a relationship to true leukemia."

Interrelations of the Hyperplastic and Neoplastic Diseases of the Hematopoietic System.—The voluminous literature relating to the diseases of the hematopoietic system characterized by hyperplastic changes gives evidence of our inexact and incomplete knowledge of these processes. There has been too great a tendency to delimit as definite entities conditions which show only minor and non-essential variations from supposed classical types. This has led, in its turn, to additional literature whose aim has been an attempt at correlation and unification. The difficulty of arriving at a conception which will homologize the various conditions in which hyperplasia of the hematopoietic tissue occurs is due, in part, to the many unexplainable variations which individual cases may exhibit, and, in part, to our still incomplete knowledge of hematopoiesis. We can attempt the more precise limitation of a relatively small number of types, into which the various conditions shall fall. But as soon as such a classification is made, it is upset by individual cases which do not fit clearly into any established group but form transitions between the artificially made groupings. Or we may attempt the broader plan of trying to fit all possible variants into a single, more comprehensive scheme which looks upon tissue hyperplasia as the fundamental and common process. The difficulty with the latter concept, which is the ideal one, is our inability to decide where hyperplasia ends and neoplasia begins, and to define hyperplasia as a process distinct from neoplasia. Perhaps it is the tendency which tries to draw a sharp distinction between these two processes as they occur in the hematopoietic system which is at the bottom of our difficulties. Possibly it would be better if we looked upon non-invasive hyperplasia and invasive proliferation of the parenchymatous elements of the hematopoietic system as the extremes of an identical process, common to all stages of which is the unknown etiology. It is particularly in infancy that this process manifests the greatest degree of variability, possibly because the instability and lability of the hematopoietic system at this early age permit a return to an active, fetal condition as a reactive response to a variety of causative factors.

If we attempt to analyze the hematopoietic diseases from this viewpoint, we can start with the non-invasive hyperplasias, of which the usual forms of leukemia are the best examples. Since the system of blood forming organs contains several tissue elements which are to be looked upon as the parenchyma of that system, the hyperplasia may be one of lymphocytes, myelocytes, plasma cells, or cells so young and undifferentiated that their origin can not be determined. Furthermore, if we accept the unitarian doctrine of the participation of the reticulo-endothelial system in hematopoiesis, then the diffuse hyperplasias of this system can be included in the group of hematopoietic system diseases. A number of writers hold extra-medullary reticulo-endothelial proliferation to be an essential element in myeloid leukemia, and Waugh and MacIntosh[120] have recently defined Gaucher's large cell splenomegaly as a "primary, probably congenital, progressive systemic disease of hematopoietic tissues, characterized by aleukemic dysmyelosis." The local multiplication of cells may or may not be associated with the escape of the cells into the blood stream. While the leukocythemic or aleukocythemic character of the process may lead to sharp clinical differentiation, the change occurring within the tissues may be an identical one. The usual form of leukemia and the aleukocythemic form (pseudoleukemia) would then be variants of the same condition, which could be classified clinically according to its leukocythemic or aleukocythemic nature and anatomically according to the cell type taking part in the hyperplasia.

The non-invasive hyperplasia of leukemia bears a resemblance, on the one hand, to the hyperplasias which may develop as the result of infection, inflammation or toxemia. Some of these conditions, especially in children, may be associated with an absolute increase in the number of circulating leukocytes or with a relative increase of certain of them, as marked as occurs in some of the leukocythemic leukemias and certainly greater than that of the aleukocythemic forms. At the other extreme, the leukemias pass over imperceptibly into the invasive hyperplasias with a typical leukocythemic blood picture, the leukosarcomatosis of Sternberg, and those without such hematologic findings, the lymphosarcomatosis of Kundrat and Paltauf. Diffuse leukocythemic hyperplasia with exophthalmos and deafness due to predominating involvement of the skull, but with no green coloration of the tissue, is identical with chloroma in all respects except color. Chloromatous hyperplasia, with leukocythemia and without skull or other local tumors, is identical with the usual form of leukemia except in the color of the tissue. Aleukocythemic chloromas, with and without local tumors, have been reported. That the color is not an essential characteristic of chloroma is indicated by a case reported by Schmidt.[121] An enlarged axillary node removed for diagnostic purposes was colorless; at necropsy eight months later all the enlarged lymph-nodes had a green color. Within the chloroma group the hyperplasia may be lymphocytic, myelocytic, myeloblastic, or plasmacytic, and it may exhibit varying degrees of invasiveness. For the invasive forms Sternberg[103] proposed the name chlorosarcomatosis or chloromyelosarcomatosis in order to homologize them with his leukosarcomatosis. Neither the entrance of cells into the blood stream, the degree of invasiveness, or the color of the tissue, therefore, permits any sharp distinction within the great group of diffuse hyperplasias of the hematopoietic system. All should be combined under the single head of what the Germans term a "*Systemerkrankung*" of this system, as stages or variants of a single essential pathologic process. Whether we think of this process in terms of hyperplasia or neoplasia is a matter of lesser moment.

Typical leukemia, with its chloromatous and sarcomatous variants, is a process which involves the hematopoietic system diffusely, but it does not involve all the elements of this system. There have been reported cases with characteristic leukocythemic changes, but with non-invasive hyperplasia limited to a portion of the hematopoietic system, a single group of lymph-nodes, usually the mediastinal, or more rarely the spleen or some portion of the bone marrow. Similar localized hyperplasias, but aleukocythemic in character, have also been described. These appear to give the transition to the aleukocythemic myelomas, which may be, as already noted, myelocytic, lymphocytic or plasmacytic. In the myeloma group there are varying degrees of invasiveness. In Sternberg's leukosarcomatosis group have been included cases with invasive tumors limited to the mediastinum. The aleukocythemic lymphloblastoma, which begins in some localized region and then metastasizes to other portions of the system and to other organ systems, illustrates the most extreme grade of invasiveness. It appears proper to conclude, therefore, that neither the diffuse nor localized character of the hyperplasia permits distinctions based upon this character alone. The localized overgrowths should find a place under the single heading which includes the diffuse hyperplasias.

A classification which attempts to bring together the various hyperplastic diseases of the hematopoietic system was proposed by Pappenheim,[122] and is given below. A criticism which may be made against it is that it does not go far enough, in that Pappenheim found it advisable to make two main divisions whose basis is the non-invasive or invasive character of the hyperplasia. The non-invasive conditions he grouped together under malignant hyperplasia, and for each variant under this heading there was a homologue under blastomatous or sarcomatous hyperplasia. The formulation of a mental conception of malignant hyperplasia, as distinguished from blastomatous hyperplasia, is difficult, particularly in view of the fact that the one feature which Pappenheim attempted to emphasize was the transition of one into the other. Since his aim was unification, Pappenheim's classification would be improved if, while retaining its double column feature simply to illustrate the extremes of hyperplasia, it did away entirely with the two words malignant and blastomatous for the extremes of the process, since we can make no precise definition of these words. In the Pappenheim classification which follows, the subheads in brackets are additions made by the writer.

I. Malignant Hyperplasia:	II. Blastomatous Hyperplasia:
1. Lymph-nodes and spleen chiefly involved. Lymphatic pseudoleukemia. Clinically aleukocythemic.	1. Lymph-nodes and spleen: (*A*) Aleukocythemic lymphosarcomatosis (Kundrat) (*B*) Sarcoleukemia. Lymphoblasts or macroleukocytes in circulating blood.

2. Bone marrow involved:
    - (*A*) Aleukocythemic:
        - (*a*) Localized (Myelomatosis):
            - Lymphocytic
            - Myelocytic
            - Plasmacytic
            - [Erythroblastic]
        - (*b*) Diffuse. Myelopathic anemia (medullary pseudoleukemia of other authors). Usually lymphocytic.
    - (*B*) Leukocythemic:
        - (*a*) Leukemia:
            - Lymphoid
            - Myeloid
            - [Macrocytic. Large undifferentiated mononuclear cells, whose lymphoid or myeloid origin cannot be determined.]

2. Bone marrow:
    - (*A*) Aleukocythemic:
        - (*a*) Localized (Sarcomyeloma):
            - Lymphocytic
            - Myelocytic
            - Plasmacytic
            - [Erythroblastic]
        - (*b*) Diffuse. Lymphadenia ossium (only one case described, that of Nothnagel).
    - (*B*) Leukocythemic:
        - (*a*) Myelosarcoleukemia:
            - Lymphoid
            - Myeloid
            - [Macrocytic]

Epiblastic Hylic Tumors.—The neuroblastomas and the glioblastomas, the former involving chiefly the sympathetic nervous system and the latter chiefly the central nervous system, constitute the malignant hylic tumors of epiblastic origin.

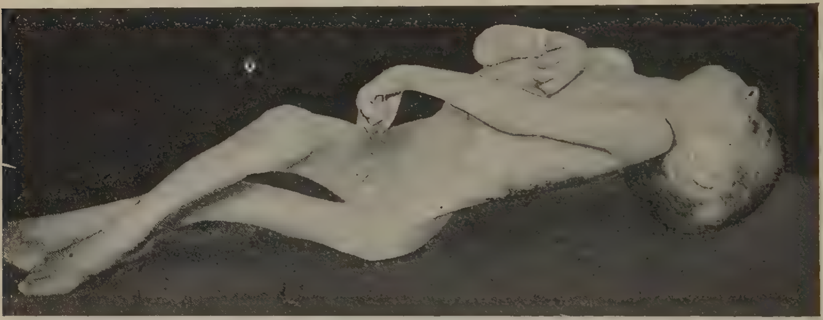

Fig. 327.—Opisthotonos and emaciation in glioma of the brain. (Collection of Dr. I. A. Abt.)

The characteristics and localization of neuroblastoma have been sufficiently discussed above. Concerning the glioblastoma it is only necessary to add a few data relating to distribution. This tumor occurs only rarely in the spinal cord, but in the brain is one of the most frequent tumors of childhood. Steffen's[123] collection included 80 tumors of the brain and meninges. The exact histologic diagnosis is not clear in many of these; those which were reported as round-cell sarcomas of the brain itself were probably all glioblastomas. A few certainly benign gliomas were also included, but since the distribution of these is the same as that of the glioblastomas they may be included among the latter. Among Steffen's eighty tumors were 53 probably gliomatous and glioblastomatous tumors of the brain. Thirty-one of these were in males, 16 in females, and in 6 the sex was not stated. Fourteen occurred in the cerebrum and basal ganglia, and 39 in the cerebellum, pons and fourth ventricle. In the case of the cerebellar tumors, the vermis and left lobe were primarily involved with equal frequency and more often than the right lobe. In one case of cerebellar glioblastoma the entire cord was also involved. Wollstein and Bartlett's[124] smaller group of nine gliomatous tumors in children from two weeks to three years of age showed the same preponderance of males over females, the proportion being seven boys to two girls. Of seven of these tumors studied in detail, five were situated in the cerebellum (subtentorial) and two were in the cerebrum (supratentorial). Symptomatically glioblastoma is not to be differentiated from glioma or any other form of brain tumor. Localization is sometimes possible from the symptoms, but the latter are often rendered indefinite by hydrocephalus. Opisthotonous may be marked, and the brain tumors of children may be associated with more extreme grades of wasting than one sees in any other condition (Fig. 327).

Hypoblastic Hylic Tumors.—The only malignant hylic neoplasm of hypoblastic origin is the rare chordoblastoma. The recent collective studies on chordoblastoma of Linck and Warstat,[125] Stewart,[126] Andler and Schmincke,[127] and Coenen[128] show that this tumor has been encountered almost without exception in adults, being frequently associated with a history of trauma. The tumor reported by Fabricius-Möller[129] in a male aged 16 years was situated in the posterior wall of the pharynx and measured 4 by 2 cm. It had been present for seven years, had increased in size during the latter part of its course, and recurred after removal.

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Malignant Lepidic Tumors

The group of malignant lepidic tumors is composed of the epitheliomas and carcinomas derived from surface or glandular epithelium of epiblastic, hypoblastic or mesoblastic origin, and of the endothelioblastomas of mesoblastic origin. All are characterized, in typical examples, by a distinctly alveolar arrangement, the aggregates of tumor cells being separated from each other by stroma which may vary in amount and in density. The cells within the alveoli are in immediate contact with each other and are not separated by supporting fibrils. While the alveolar character is the distinguishing and most striking feature of this group of neoplasms, it may be so indistinct in some tumors that differentiation from the malignant hylic tumors becomes difficult or impossible. It is especially the epithelial and endothelial neoplasms of mesoblastic origin which show this tendency to diffuse, non-alveolar growth. The sarcoma-like growth of the mesoblastic lepidic tumors is believed by Adami[1] to be due to the fact that the middle germ layer is originally a hylic tissue, in which the formation of epithelial and endothelial lepidic tissues is the result of later differentiation. The tumors derived from such tissues may, therefore, dedifferentiate to such a degree that they lose the lepidic character which was a secondary development of their ancestors, and return to the original hylic condition of the earliest mesoblastic cells. For this reason, Adami found it necessary to place the lepidic mesoblastic tumors in a subgroup which he termed the transitional lepidomas.

Malignant Epithelial Tumors.—While collective statistics bear out the dictum that the carcinoma is a tumor of adult life, it occurs frequently enough in the early years of life to make it necessary to keep in mind the possibility of carcinoma in every tumor of childhood. The relative frequency of carcinoma in childhood, as compared with the same tumor in adults and with mixed and hylic tumors during childhood, has already been discussed. The total of 87 cases of carcinoma in children collected by Philipp[2] in 1908 was increased to 111 by Merkel[3] in 1912. The organ distribution of these tumors was as follows: Large intestine 28; ovary, 25; skin, 16; liver, 13; stomach, 7; adrenal, 5; pancreas, 5; testis, 3; buccal cavity, 2; hypophysis, 2; small intestine, kidney, larynx, uterus, thyroid, each 1.

Epithelioma.—We shall reserve the term epithelioma for malignant tumors of squamous epithelium. Such tumors may be derived from the surface epidermis; from the epithelium of the lower genito-urinary tract (renal pelvis, ureter, urinary bladder, urethra, vagina); from that of the upper alimentary and respiratory tract (buccal cavity, tongue, larynx, trachea, esophagus); in the hypophyseal region from remnants of Rathke's pouch; and in the neck from persistent branchial cleft epithelium. In certain situations, as the lung, metaplasia of normal columnar epithelium to squamous epithelium may be associated with the formation of typical epithelioma in an organ which does not normally contain squamous epithelium. The epitheliomas of surface membranes may have a markedly papillomatous character, and they may arise in previously benign papillomas. When such papillomatous tumors are definitely malignant there is always evidence of invasive downward growth into the stroma, with the formation of solid alveoli composed of cells of squamous type.

Epithelioma of the skin in children is of some interest because of its relation to chronic inflammatory processes and because of the familial tendency sometimes apparent. Merkel[3] mentions Braun's case of epithelioma, in a girl 12 years old, which developed in the scar of a burn which had occurred when the child was two years old. Roth[4] has reported a basal cell epithelioma of the skin of the gluteal region of a girl aged 11 years. The tumor, which was ulcerated and 4 to 5 cm. in diameter, arose at the site of a penetrating injury to the skin by a thorn sutained eight months previously. Multiple epitheliomas may develop in the chronically inflamed skin of xeroderma pigmentosum; most of the reported cases of familial epithelioma have occurred in this disease. Rüder[5] noted the occurrence of multiple epitheliomas of the skin in 7 of 8 brothers belonging to a family of 13 children. The atrophic and pigmentary changes in xeroderma and its familial occurrence suggest a developmental anomaly. Rich, Davison and Greene,[6] who made a histologic study of the skin in a case of xeroderma pigmentosum in a boy aged 4½ years, believed the action of sunlight, in a predisposed individual, to be a primary factor in the epithelial hyperplasia. They compared the reaction in the skin to that which may follow exposure of the skin to the roentgen-ray.

In other instances malignant epithelial tumors of the epidermis have had no apparent relation to trauma or inflammation. Warthin's[7] series of tumors in children included one example each of epithelioma of the ear, leg, mouth, and eye. Lippe[8] reported an epithelioma of the face in a four year old girl; the tumor arose in a wart-like growth which had been present for three months. Étienne and Aimes[9] reported an epithelioma of the scalp of a boy aged 14 years; the tumor had already reached such a size when it came under their observation that it was inoperable. Battle and Maybury[10] described an epithelioma of the nipple in a girl aged 11 years. In the records of St. Thomas' Hospital, London, they found one other example of malignant epithelial tumor at an early age, an epithelioma of the lip in a boy aged 14 years; removal was followed by recurrence and death. Stephen[11] reported an epithelioma of the lip, which was first noticed when the patient, a boy, was 12 years old. Removal was followed by recurrence within three months and by metastases in the cheek and in the submaxillary and submental lymph-nodes of both sides. The rarity of epithelioma of the lip in the early years of life is illustrated by Broders'[12] statistics from the Mayo Clinic; in this series of 537 such neoplasms, there was none under 21 years of age.

Epithelioma of other situations where squamous epithelium normally occurs is rare in children. Merkel's[3] table includes such a tumor of the larynx; this is probably the cancroid of the larynx in a boy three years old reported by Rehn[13] in 1868. The tongue, esophagus, urinary bladder, and vagina are apparently only extremely rarely the seat of epithelioma during childhood. Hadda[14] found no examples of epithelioma of the bladder under 20 years of age in a series of 48 such tumors occurring among a total of 5006 cancers. In 65 primary bladder tumors in the first decade of life, tabulated by Deming[15] in 1924, there was only one papilloma, and no epithelial tumor listed as malignant. Stadler[16] reported an unusual bladder neoplasm in a boy aged two years. Difficulty in urination, which had already been present during the first year of life, ended in retention. Cystoscopic examination revealed numerous small, pedunculated, polypoid growths attached to the posterior wall of the bladder. Removal of these was followed by a return of symptoms, requiring a second operation, at which the bladder was found filled with similar tissue. The latter consisted of myxofibromatous stroma covered by hyperplastic, multilayered epithelium of the type of epidermis. Recurrence and death followed the second operation. Thomas[17] has described a papillary epithelioma of the pelvis of the kidney in a girl aged 3½ years; death from recurrence followed nephrectomy. Erdheim[18] considered malignant two epitheliomatous tumors derived from Rathke's pouch, occurring at the ages of 11 and 16 years.

Rosenbusch* has recently described as a carcinoma solidum simplex a tumor in a male infant 1¼ year old. It arose in the nasopharynx, apparently from the surface epithelium, and from its description was an epithelioma. It penetrated the sphenoid to the middle cerebral fossæ, appeared externally beneath the skin on each side of the head between the zygoma and the ear, and metastasized to both adrenal regions. A similar tumor, in a boy aged 6 years, is credited to Jeanneret.

Carcinoma.—The malignant epithelial tumors of glandular origin have received a variety of names of descriptive purport: Adenocarcinoma, if the glandular character of the neoplasm itself is very marked; medullary or encephaloid carcinoma if it is highly cellular, with relatively little stroma; scirrhous, if the stroma predominates; colloid, if mucinous secretion is present. Tumors derived from the specialized epithelial parenchyma of certain organs have been given special names, as hypernephroma, hepatoma, etc. Having reserved the term epithelioma for the malignant squamous epithelial tumors, we shall refer to those of glanular origin simply as carcinomas, since such features as glandular character, stroma content and cellularity may vary in tumors of identical origin. According to the combined figures of Philipp[2] and Merkel,[3] the gastro-intestinal tract is more frequently the seat of carcinoma in childhood than any other organ system. With the increasing number of reported epithelial tumors of the liver, ovary and adrenal, it is possible that the older statistics may have to undergo revision.

Stomach.—Osler and McCrae,[19] in their monograph "Cancer of the Stomach" published in 1900, devoted a chapter to "cancer of the stomach in the young." A critical search of the literature revealed six previously reported cases below the age of 10 years, and thirteen during the second decade. Of the six early cases, four were infants under six weeks of age, one was a child aged 18 months, and one a boy of eight years. Two of these, Williamson's case dying at five weeks of age and Kaulich's at the age of 18 months, appear quite doubtful. The first, in which microscopic examination was not made, appears to have been an example of pyloric hypertrophy, and in the second case it could not be positively determined whether the tumor was primary or secondary in the stomach. A third case, reported by Widerhofer in an infant 16 days old, was also possibly a secondary carcinoma of the stomach. In the case of an eight year old child, recorded by Ashby and Wright, there was an ulcerated cavity on the duodenal side of the pyloric sphincter as well as two small nodules above the sphincter; it is possible that the larger, ulcerated duodenal lesion may have been the primary carcinoma. Of this group of six supposed gastric carcinomas early in life, included without question by those who have followed Osler and McCrae in spite of the reservations which the latter themselves made, the most interesting and certain is that of Cullingworth.[20] Vomiting began when the child was 10 days old and continued until death, which occurred 29 days later. The pyloric orifice was filled by a soft, ulcerated tumor an inch long; histologically this was a cylinder-cell carcinoma. Of the Osler and McCrae group of thirteen cases during the second decade, one occurred in a girl aged 13 years, one in a boy aged 14 years, one in a boy of 15 years, and one in a boy aged 16 years; the rest were all above the latter age.

The Philipp-Merkel series included only eight cases of carcinoma of the stomach at 15 years or under; no new cases had been added to the Osler and McCrae series. Sullivan,[21] in 1924, increased the number of gastric carcinomas, in children 16 years old or under, to twelve. In this series there were nine males and one female; in two cases the sex was not stated. Special interest attaches to the case reported by Ghon[22] in a boy aged 13 years; the carcinoma, which was situated on the lesser curvature, developed in a chronic ulcer due to the swallowing of lye. Karl[23] reported as cured by resection a carcinoma of the pylorus in a boy aged nine years; a post-operative observation period of three months, during which the child remained well and increased in weight, is probably too short to determine the question of cure. The case of carcinoma of the stomach in a new-born infant which Merkel[3] credits to Leube and Wilkinson is the Williamson case of probable pyloric hypertrophy of the Osler and McCrae series. Perhaps the numerous incorrect references to this case and the grave doubt as to its carcinomatous nature are due to the fact that it was published in 1841. Common to the gastric carcinomas at early ages is the rapid clinical course. According to Schlesinger,[24] the entire duration from initial symptoms to death was only two weeks in a girl aged 14 years, three weeks in a girl aged 17 years, and a "few weeks" in a boy aged 15 years.

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* Ueber das Karzinom des Nasenrachenraumes im frühen Kindesalter, Frankf. Zeitschr. f. Path., xxxi (1925), p. 507.

Intestine.—Carcinoma of the intestine is situated, as a rule, in the large intestine. Merkel's[3] series of 28 cases of intestinal carcinoma in children 15 years old or under includes only one of the small intestine, a carcinoma of the duodenum in a boy aged 3½ years. To this should probably be added the Ashby and Wright case of the Osler and McCrae[19] series of stomach carcinomas. In the large bowel, the rectum and sigmoid are most often involved, the former thirteen times and the latter seven times in Merkel's series. Phifer[25] collected and tabulated 49 cases of carcinoma of the rectum and sigmoid in individuals under 20 years of age. Twenty-three of these were males and 13 were females; in 13 the sex was not stated. The age distribution was as follows: Under one year, 1 (a monster); one to five years, 0; 6 to 10 years, 1; 11 to 15 years, 22; 16 to 20 years, 25. The intestinal carcinoma reported by Saint-Jacques and Parizeau[26] occurred in a boy aged 11 years; its course had been asymptomatic until the sudden onset of intestinal obstruction. The tumor involved the intestine for a length of four inches. Von Muralt[27] reported a case of multiple carcinomas of the intestine in a boy aged 13 years. Symptoms present for four years had led to a probable diagnosis of tuberculous peritonitis; laparotomy, made necessary by sudden obstruction, was followed by death in two days. The whole intestinal tract was found studded with tumor nodules, the largest being in the ascending colon; the tumors were typical cylinder-cell carcinomas, with areas of colloid change. Milne[28] reported a constricting colloid carcinoma of the upper part of the rectum in a boy aged 12 years; metastases were present in the perirectal lymph-nodes. In spite of the relative frequency of adenomatous polyps of the large intestine in children, a history indicating the previous existence of such a polyp is rarely obtained in the intestinal carcinomas. The carcinomas of the gastro-intestinal tract of children do not differ histologically from those of adults. The cells which line the gland-like acini may vary from cuboidal to columnar in height, and may vary greatly in shape. The tumors metatasize to the mesenteric lymph-nodes, liver and pancreas.

Ovary.—In the ovary, which, according to Merkel,[3] ranks next to the gastro-intestinal tract in frequency of involvement, the malignant tumor may arise in a papillary cyst, or more rarely may begin as a solid tumor. In the latter it is not always easy to exclude origin from a solid teratoma and undoubtedly a certain number of embryonal carcinomas developing on a teratomatous basis have been included among the primary ovarian carcinomas. The incidence of ovarian carcinoma increases markedly during the second decade, that is, at and just after puberty, as compared with the first decade. Of 25 cases accepted by Merkel, only four occurred during the first decade. Wiel,[29] who reported the occurrence of a large, partly cystic carcinoma of the ovary of a girl aged five years, was able to find four examples of ovarian carcinoma at 10 years of age or under in the literature previous to 1905. These occurred in a total of 61 ovarian tumors distributed as follows: Teratoma and dermoid, 23; cyst, 19; sarcoma, 15; carcinoma, 4. Four years later Edwards[30] called attention to the increasing number of reports of malignant disease of the genitalia in girls, and tabulated 50 cases of malignant tumor of the ovary in girls 16 years old or under. Fourteen of these were carcinomas, the age distribution being as follows: In a seven months fetus, 1; at one year, five years, and seven years, 1 each; at 8 years, 3; at 9 years, 2; at 13 years, 1; at 15 years 2; at 16 years, 1; exact age not stated, 1. An additional case, at 13 years of age, was listed as a sarco-epithelioma. Wiel called attention to the sarcoma-like character of his tumor and to the difficulty of establishing the carcinomatous nature of certain ovarian tumors almost certainly of epithelial origin. Later reports of single cases of ovarian carcinoma of children have been made by Rosanoff,[31] Lahey and Haythorn,[32] Knott,[33] Gerson,[34] Ridout,[35] and others. In Lahey and Haythorn's case, a girl aged 11 years, both ovaries were involved, and in Gerson's case, a girl aged nine years, the second ovary became involved by metastasis after removal of the primary tumor. The occasional association of sexual precocity with ovarian tumors, the latter including the carcinomas reported by Reuben and Manning,[36] and Knewitz,[37] has been discussed in the section on abnormal development due to tumors.

Uterus.—In his tabulation of 32 malignant tumors of the uterus, occurring at at the age of 15 years or earlier, Edwards[30] included seven cases of carcinoma, one each at two years, 2½ years, 8 years, 10 years, and 14 years, and two at 13 years. Of this group of cases, those at 2, 8 and 14 years arose in the cervix, but were glandular or medullary in character. An additional case included by Edwards, in a girl aged two years, was described as a carcino-sarcoma. In the carcinoma of the uterus of a child aged 2½ years recorded by Adams,[38] the entire body and cervix had been replaced by a tumor of glandular character, which had penetrated the bladder.

Mammary Gland.—Carcinomas of the female mammary gland have been reported by Thompson[39] in a girl aged 11 years; by Levings[40] in a girl aged 12 years; by Martin[41] in a girl of 14 years; and by Brewer[42] in a negro girl 16 years old. In Brewer's case, a small, painless lump, which had been present as far back as the girl could remember, increased in size during the final period of six months; the tumor was an intracystic adeno-papilloma which had become malignant. In a remarkable case reported by Blanc[42a] the tumor appeared shortly after birth and within a few months had spread to the axilla and into the hypochondrium and was inoperable. Carcinoma of the male mamma also occurs during childhood. Blodgett,[43] in 1897, reported a carcinoma of the mamma of a boy aged 12 years; the report was made five years after operative removal of the tumor, up to which time there had been no evidence of recurrence. Simmons[44] described as an adeno-carcinoma of medullary type a tumor of the breast in a boy aged 13 years; the photomicrographs are not very convincing and are more suggestive of interstitial fibrosis with duct hyperplasia. Schneller,[45] in a monographic resumé of the pathology of the male mamma published in 1922, refers to a case of carcinoma of the breast in a boy aged 10 years, reported by Yamamoto, who could find only four cases under 20 years of age in a total of 245 cases of male mammary carcinoma. Blanc[42a] has recorded a carcinoma of the mamma in a male infant, very similar to his mammary tumor in a female infant mentioned above. In the male infant the mamma had begun to enlarge shortly after birth, and at the age of six months the axilla was invaded. Radical operation was followed by hemoptysis, supposedly due to lung metastases, and by death three months after the operation.

Liver.—Primary carcinoma of the liver in adults has formed the subject of a number of important monographic dissertations during the past two decades, and this neoplasm no longer holds its earlier place as one of the pathologic rarities. Primary epithelial tumors of the liver are also not especially infrequent during childhood, but it is not always easy to determine the malignant character of these neoplasms from their histologic structure. They are usually composed of cells which imitate rather closely the parenchyma of the liver, tend to be arranged in solid cords but not in lobules, and form bile capillaries which contain bile. The tumors are usually encapsulated, which characteristic, together with the morphologic differentiation of the cells, has often led to their inclusion among the benign epithelial tumors under the designation of hepatoma. In spite of their encapsulation, they may form secondary nodules within the liver and metastases in the peritoneum and in distant organs. Their growth is progressive and becomes associated with the formation of atypical cells which have invasive properties.

Philipp,[2] in his tabulation of carcinomas of childhood published in 1907, included 29 tumors of the liver. Twelve of these he considered certain examples of primary carcinoma, 10 probable, and 7 uncertain. Castle,[46] in 1914, added 13 cases from the literature and 1 of his own to Philipp's 29 cases. His case, in a boy aged 10½ months, was unusual in that the tumor was encapsulated, pedunculated, but rather broadly attached to the inferior surface of the liver. It could be completely excised, but death occurred with symptoms of acute gastro-enteritis 14 days after operation. The microscopic diagnosis was parenchymatous adenocarcinoma. Griffith,[47] in 1918, again reviewed the subject in connection with a tumor of the liver reported by him in a girl aged 21 months. The neoplasm, which was considered inoperable upon exploratory laparotomy, was about the size of an orange; it was encapsulated and did not appear to infiltrate. The microscopic diagnosis of a bit of the removed tumor tissue was carcinoma simplex; the tubular arrangement was suggestive of an origin from bile ducts. Griffith brought the total number of reported cases, including his own, to 57. Of this number, 25 were males and 26 were females; in 6 the sex was not stated. In 2 cases the age was not given, but the remaining 55 were all under 16 years of age, the age distribution being as follows: New-born, 4; 1st year, 12; 2nd year, 8; 3rd year, 2; 4th year, 2; 5th year, 2; 6th year, 2; 7th year, 2; 8th year, 1; 9th year, 3; 10th year, 1; 11th year, 4; 12th year, 5; 13th year, 1; 14th year, 3; 15th year, 2; 16th year, 1. Other cases reported by Frölich,[48] de Saussine, Androutsellis and Bertrand,[49] Hattery,[50] Wollstein and Mixsell,[51] bring the total of cases of primary carcinoma of the liver in children to rather formidable proportions. It is to be noted that both Castle and Griffith start with 29 cases collected by Philipp, who himself accepted only 12 of these as certain; and both include tumors reported as adenomas or benign hepatomas by the original authors. Since it is not always possible to decide the question of malignancy in the liver neoplasms upon the basis of gross or microscopic features, it is probably just as well to include all under one heading as potentially malignant.

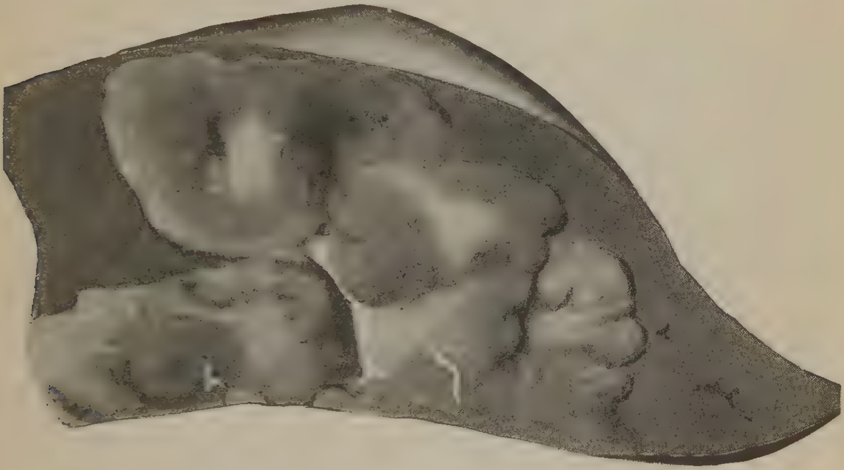

FIG. 328.—Carcinoma of liver. (Collection of Dr. I. A. Abt.)

Although most of the primary epithelial liver tumors of childhood are apparently derived from liver parenchyma, a few of the reported neoplasms have had a structure which suggested an origin from bile ducts. Such tumors, an example of which was recently described by Dansie[52] in a 10 weeks old infant, have a more glandular or tubular character, and contain a large amount of stroma. Jaundice and ascites, which are rare or terminal manifestations of the parenchymatous type, are more prominent in the biliary form. These differences are well illustrated by two tumors of the liver in children included by Karsner[53] in a series of nine primary carcinomas of the liver studied by himself. Of these, one occurred in a girl aged 11 years; the tumor was of glandular or tubular type and was believey to have originated in the bile ducts. Jaundice and marked ascites were noted during life, and the tumor was associated with cirrhosis. In the second case, a bod aged eight years, the tumor was of the solid, parenchymatous type. There had been no jaundice or ascites, and the tumor had not led to cirrhosis. Karsner proposed the names carcinoma adenomatosum for the tumor of biliary duct origin, and carcinoma solidum for the parenchymatous type. Forman and Hattery suggested the names carcinoma cholangio-cellulare and carcinoma hepaticellulare. Cirrhotic liver changes were recorded in only three of the cases tabulated by Castle, although an additional case was termed a scirrhous carcinoma. The typical symptoms of primary carcinoma of the liver in children were given by Castle as follows: cachexia and anemia; abdominal tumor; pain; icterus, if the tumor occludes bile ducts by pressure; ascites, if obstruction to portal or lymphatic circulation occurs; and terminal fever.

A tumor of the liver which differed in certain respects from the usual form of carcinoma of the liver was described by Holt[54] as a primary adenosarcoma. It occurred in a boy aged nine months, and was found to be inoperable upon exploratory laparotomy. It was fluctuant and was incised and drained. At necropsy most of the tissue was made up of atypical liver cell columns, but there were also groups of small, deeply stained cells, which were considered sarcomatous. The conclusion was drawn that the tumor had begun as a liver cell adenoma, to which sarcoma was added at a later date. Since the tumor was necrotic and had been drained, it is difficult to exclude secondary lymphocytic invasion. It is probable that examples of embryonal carcinoma developing in teratomas have also been included among the primary liver cell carcinomas; Castle included Yamagiwa's[55] tumor of a one year old girl, which was carcinomatous, but contained bone.

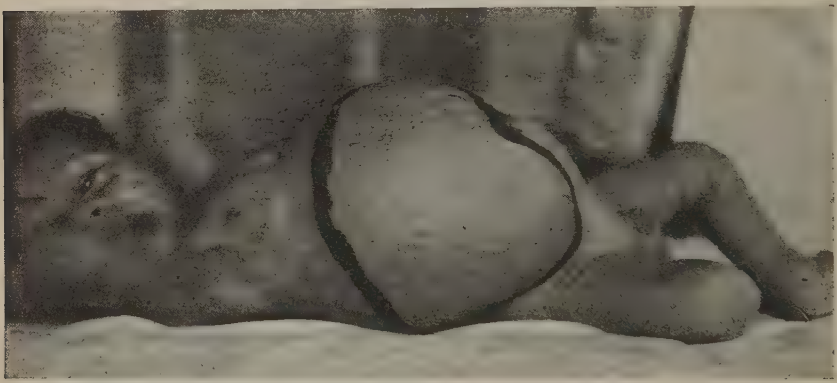

FIG. 329.—Abdominal enlargement due to carcinoma of liver. (Collection of Dr. I. A. Abt.)

Lung.—Horn[56] reported a carcinoma of the lung in a girl who had had symptoms referable to the lung since the age of 14 years. At this time she began to complain of cough, pain in the chest, and dyspnea; tympany was present over the upper portion of the left lung. Hempoptysis set in and death occurred at the age of 18 years. The main bronchus of the shrunken, fibrotic left lung was filled with pale tumor tissue, which extended into one of the bronchial branches for a distance of 4 to 5 cm. The tumor tissue did not invade deeply, but remained closely confined to the involved bronchi. It had a markedly alveolar, glandular character, and was believed to have arisen from the columnar epithelium of the bronchial mucosa; some of the tumor cells were ciliated. Horn quotes Benckert's statistics of 90 cases of carcinoma of the lung. Among these there was one at seven years and one at 15 years, both being females.

Hypernephroma.—In the adrenal, neoplasms arising from and composed of cortical tissue may be associated, especially in girls, with the anomalies of development already considered above. These tumors illustrate well the sarcoma-like character of the neoplasms derived from mesoblastic epithelium. They have often been recorded either as large round-cell sarcoma or perithelioma, but are probably all derived from the glandular parenchyma of the cortex. The occurrence of hypernephroma of the ovary, associated with sexual precocity, has been reported by Gaudier[57] in a girl aged five years, by Downes and Knox[58] in a girl aged 3½ years (Fig. 330), and by Debeyre and Riche[59] in a girl aged four years. Misplacement of adrenal cortical tissue into the kidney is not infrequent, but the development during childhood of malignant hypernephromas from such misplacements occurs only rarely. In a total of 106 hypernephromas of the kidney collected by Cutler,[60] there was only one such tumor during the first decade and none during the second. Fischer[61] reported a hypernephroma of the left kidney in a boy aged 11 years; as is the rule in the renal hypernephromas of adults, hematuria was a symptom. Reinmann[62] reported a melanotic carcinoma of the adrenal in a three months old child. Maclachlan,[63] who reported a bilateral melanosarcoma of the adrenals in an adult, could find no previously recorded example of this rare kind of neoplasm in children. The exact nature of these pigmented tumors of the adrenal is difficult to determine; they may be examples of chromaffinoma, and belong to the group of adrenal neoplasms of sympathetic nervous system origin.

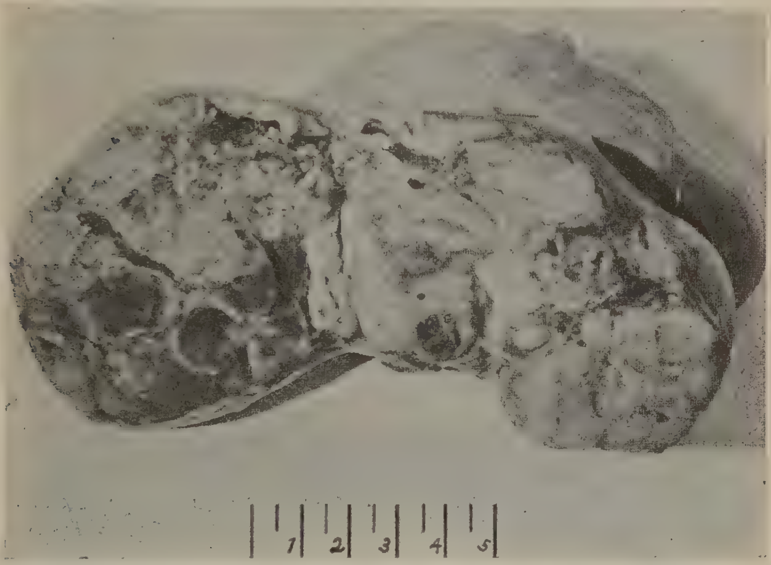

Fig. 330.—Hypernephroma of ovary in a girl aged 3½ years. (Downes and Knox.[58])

Kidney.—The occasional occurrence of squamous cell epithelioma of the pelvis of the kidney in children has already been noted. Malignant glandular tumors derived from renal epithelium are even more unusual. Ribbert[64] described as an adeno-carcinoma a tumor of the kidney in a boy aged nine years. A tumor recently removed at the Michael Reese Hospital was closely attached to and partly invaded the posterior surface of the upper pole of the left kidney of a boy aged 10 years (Fig. 331). The greater portion of the tumor was necrotic. Microscopically the tumor was a carcinoma, but of embryonal type (Fig. 332) and had

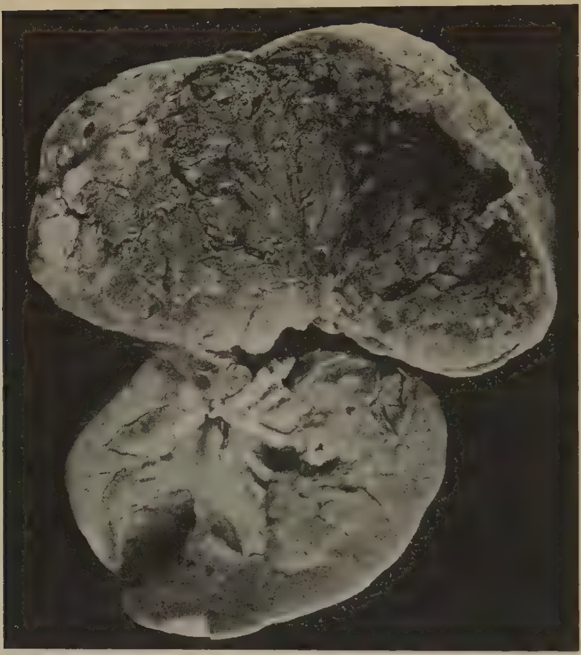

FIG. 331.—Embryonal carcinoma of kidney; boy aged 10 years.

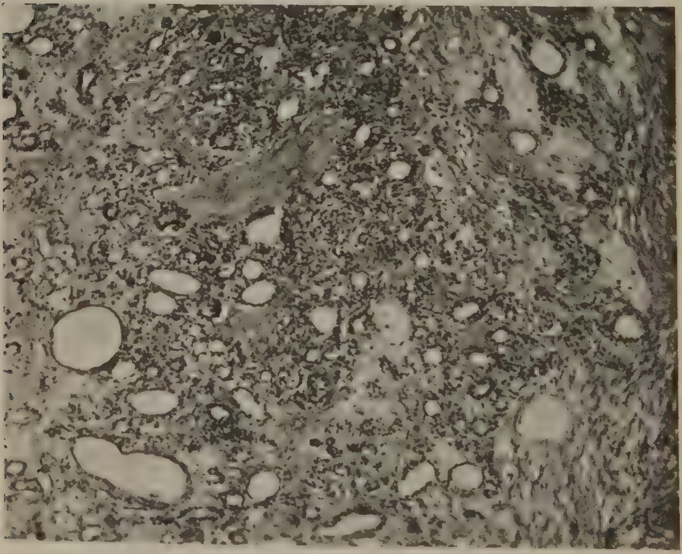

FIG. 332.—Embryonal carcinoma of kidney. ×140.

nothing in common morphologically with tumors derived from the renal parenchyma or from adrenal cortex or with the congenital renal mixed tumors. It is believed to be an embryonal carcinoma which originated in a teratoid tumor.

Testis.—In the testis of adults there occurs a medullary, cellular, large-celled tumor, concerning the origin of which there has been much discussion. It appears in the literature most often under the name of large round-cell sarcoma. Ewing[65] has held it to be the result of one-sided development of teratoma of the testis. Chevassu,[66] who derived the tumor from the germinal epithelium of the semniferous tubules, proposed the name seminoma for it. Schultz and Eisendrath,[67] who have recently reviewed the subject, concluded that the large-cell tumor of the testis is derived from the spermatocytes of the seminal tubules and suggested that it be designated spermatocytoma. If the tumor is derived from seminal tubular epithelium it belongs to the group of carcinomas. Chevassu's collected series of 59 tumors of this type contained none in children, and Merkel[3] made the statement that this neoplasm never occurs before puberty. Sacchi[68] reported as an alveolar carcinoma a tumor of the testis of a boy aged five years, associated with marked evidences of somatic and sexual precocity. Kutzmann, Gibson and Perkins[69] have reported a tumor of the testis of a boy aged 10 years, removal of which was followed within five months by widespread metastasis and death. No report of a pathologic examination of the original tumor was obtainable, but the secondary tumors were described as composed of embryonic cells with a tendency to alveolar formation. Both of these tumors were probably spermatocytomas. White[70] described as carcinoma myxomatodes a neoplasm of the testis of a boy aged 15 months, which he believed arose from the intratesticular ducts rather than from the seminal tubules. The tumor, which had compressed the body of the testis, was composed of epithelial tubules embedded in a mucoid stroma. The illustrations in general suggest a condition of interstitial fibrosis with mucoid degeneration and tubular atrophy, rather than a true neoplasm. The author's statement of the occurrence of numerous mitoses in the epithelial cells and of invasion of the stroma by the epithelial cells justify his conclusion that the tumor was malignant, although the child was well five months after the operation. If this was actually a malignant neoplasm, it was probably of teratomatous origin. White could find only three previously reported cases of carcinoma of the testis in infancy; one reported by Marsh in 1875 occurred in a child aged two years; one, termed an adenocarcinoma, was reported by Schlegtendahl in 1885 in a child 20 months old; and one was recorded by Clark in 1900, in a child aged eight months, the tumor having been first noticed at the age of 10 weeks. Clark's[71] tumor was very similar to White's. It would appear probable that all of these neoplasms were embryonal carcinomas developing in teratomas.

Thyroid.—Hughes[72] reported a metastasizing tumor of the thyroid in a girl aged 13 years. Enlargement of the middle thyroid region had been present for three years, with increased growth during the last 10 months. Three discretely enlarged cervical lymph-nodes on removal were found to be transformed into tissue of the type of papillary carcinoma of the thyroid. The thyroid tumor, which was nodular, firm and confined to the right lobe of the gland, was removed one month later and was considered on microscopic examination to be a papilliferous carcinoma. There was no evidence of recurrence three months after operation, in spite of the fact that the tumor had already invaded neighboring lymph-nodes. Hughes said that this type of neoplasm, the only case recorded in a child, is less malignant than other forms of thyroid cancer and that it shows little tendency to infiltrate; the metastases are usually local and discrete, and there is little tendency to recurrence. The relatively benign character of thyroid tumors which have all the histologic characteristics of highly malignant neoplasms is illustrated by a tumor of a girl aged 5½ years, recently seen by the writer. The markedly atypical thyroid tissue had invaded the capsule (Fig. 333) and the surrounding dense tissue in which the gland was firmly embedded, and was present in small lymph-nodes (Fig. 334) in the latter tissue. The child was still well 19 months after removal of the tumor and roentgen irradiation.

Pancreas.—To the three carcinomas of the pancreas collected by Philipp,[2] Merkel[3] added from the literature one in a child aged 1½ year and one in a child of 13 years.

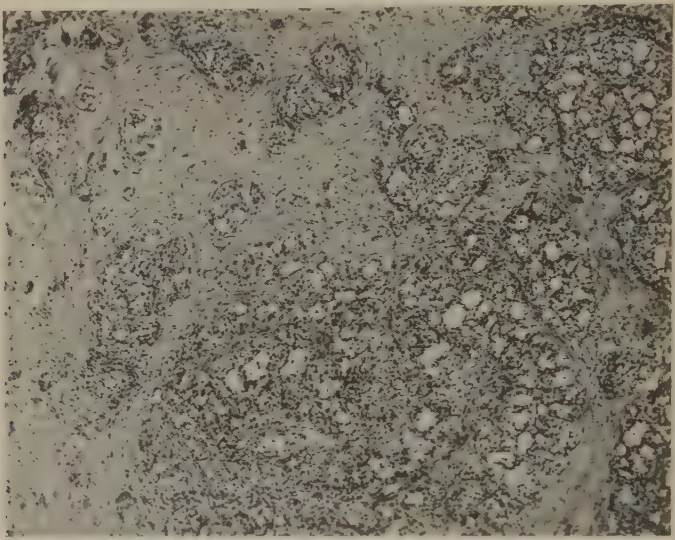

Fig. 333.—Carcinoma of thyroid in a girl aged 5½ years; invasion of perithyroid stroma. ×90.

Endothelioblastoma.—The second main division of the malignant lepidic tumors is made up of those which are composed of or derived from endothelium. The exact delimitation of this group has been a matter of contention among pathologists, which is the result not merely

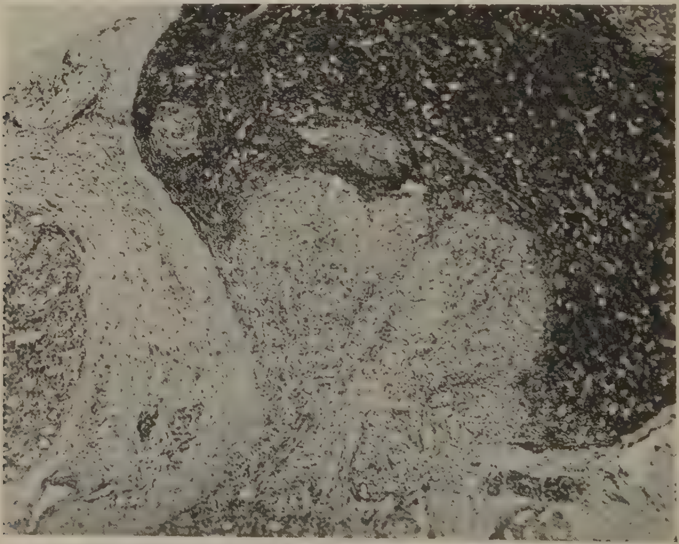

Fig. 334.—Carcinoma of thyroid; invasion of lymph node.

of difficulty in defining precisely the morphologic characteristics of the supposed endothelial tumors themselves, but to a greater degree of the inability of pathologists and cytologists to reach unanimity as to just which of the normal tissue elements are to be considered endothelia. At one extreme are those who would restrict the term endothelium to the lining cells of the lymph and blood-vessels and who would give to endothelium only angioblastic potentialities. Others would include the lining membranes of the great serous cavities and of the meningeal spaces. Still others would add the layer of flattened cells or perithelia which surround the blood-vessels of certain tissues and in places appear to form the lining of perivascular lymph spaces. Taking an extreme position are those who would include not only all the above, but would also derive from the embryonic mesoblast the cellular elements of what has been termed the reticulo-endothelial system; for these, endothelium would have not only angioblastic, but fibroblastic and hemoblastic potentialities, as well as the property of forming wandering tissue phagocytes.

Since there exists this wide diversity of opinion in regard to normal endothelium and in regard to what it may do under normal conditions, it is not surprising that pathologists should find it difficult to delimit the group of endothelial tumors and to define their characteristics. Ribbert,[64] who considered endothelium merely modified connective tissue and limited it to the linings of the blood and lymph vessels and to the coverings of the meninges, but included the so-called perithelium, believed that the endothelioma group had been widened to include many neoplasms which do not belong in it. He went even further and insisted that no tumor was to be termed an endothelioma unless its connection with or derivation from endothelium could actually be seen at some point. Borst[73] took a broader view, disregarded some of the controversial embryogenetic points, and included under endothelium all those flattened cells which have in common the property of delimiting spaces which contain blood, lymph or tissue fluids, and which may therefore be supposed to be alike physiologically, even if they may differ in origin. Borrmann's[74] attempt at classification of the tumors of endothelial origin has already been referred to above. It was based upon what he conceived to be the mode of growth of such neoplasms; it can apply only to tumors of vascular origin, and leaves out of consideration certain tumors which are morphologically neither carcinomas nor sarcomas, but come presumably from flat, space-lining cells which normally have the lepidic character of not being separated by intervening supporting fibrils. The writer believes that the endothelioma group should be broad enough to include such neoplasms. The difficulty of delimiting certain cellular, indistinctly alveolar tumors from supposed large round-cell sarcomas on the one hand, and from medullary carcinomas on the other, is admitted. In so far as confusion with sarcoma is concerned, a removal of endothelioma from the sarcoma group is desirable, even if it becomes necessary to remove from the latter all the so-called large round-cell and alveolar sarcomas and place them with the endotheliomas to prevent confusion. The distinguishing criterion of endothelioma should be its lepidic character, that is, the absence of supporting fibrils within cell groups, and the exclusion of a probable origin from epithelium. Such exclusion is not always to be made, and the lepidic character of such neoplams will place them close to the medullary carcinomas, where the endotheliomas belong if we derive them from the flattened non-epithelial cells which line spaces filled with, and cover surfaces exposed to, certain of the body fluids. One other point to be considered before taking up the discussion of the reported endotheliomas of childhood relates to the nomenclature of the malignant tumors of this group. Endothelioma has been included above under the benign lepidic tumors, the common example of the benign endothelioma being the lymphangio-endothelioma of Borrmann or the lymphangioma hypertrophicum as it is more often termed. The malignant character of a tumor of probable endothelial origin should be indicated by the terminology used. Malignant endothelioma is unwieldy and unsatisfactory. Sarcoma, the name usually applied to such neoplasms, is inexact if the hylic character is the distinguishing feature of sarcoma. In conformity with the terminology of the hylic blastomas derived from specialized tissues, proposed above, the name endothelioblastoma is suggested for the malignant neoplasms of probable endothelial origin.

Endothelioblastomas of Vascular Origin.—A few reported malignant tumors of childhood appear to answer Ribbert's requirement of demonstrated transition from vascular endothelium. De Haan[75] described, as an alveolar angiosarcoma of the liver of a child four months old, a neoplasm which appears to be such a tumor. The liver contained multiple hemorrhagic masses. Centrally these tumor nodules were composed of alveoli of smaller and larger polyhedral cells, the alveolar walls being formed by the original reticular framework of the liver. At the periphery the sinus endothelium was in active proliferation, and compressed and caused atrophy of the liver cords, which could still be recognized. The proliferating endothelium was continuous with the cells of the central alveoli. This is a type of multiple, apparently congenital tumor of the liver in young infants, other examples of which have been described by Bondy[76] under the name of angiosarcoma in a four weeks old male infant, and by Foote[77] under the name hemangioendotheliosarcoma in a boy aged three years. Foote, who considered the condition a disease characteristic of early life, collected 10 cases inclusive of his own, which he believed belonged to this group. Among the included neoplasms are those of De Haan and Bondy, as well as others by Cherwinsky, Brüchanow, Veeder and Austin,[78] and v. Falkowski.[79] In the latter the endothelial proliferation was not so marked or lawless, and such neoplasms are often included among the cavernous hemangiomas of the liver with moderate endothelial activity. All of these tumors caused progressive enlargement of the abdomen, present at birth or appearing shortly thereafter, and sometimes reaching huge proportions. All caused progressive loss of strength and death. In none were metastases formed outside the liver, except in the case of Hewlett mentioned by Foote. This case had a number of small nodules in the lungs, but their nature was not established by microscopic examination.

Similar so-called angiosarcomas may occur in the spleen. In a case reported by Böckelmann,[80] in an infant aged 1½ years, nine hemangiomas had been excised from the skin and mucous membranes at different times. The spleen had been enlarged for three months and was removed surgically. It measured 12 by 5 by 8 cm.; most of its substance had been replaced by red, angiomatous tumor tissue. The latter contained areas which were still definitely angiomatous, and other cellular, sarcomatous areas, which the author believed to be malignant. No metastases were seen at the time of the splenectomy. In a boy aged 16 years, who died of tuberculous meningitis, Golovina-Ammon[81] found the spleen enlarged to 13 by 6 by 2 cm. It contained many sharply defined, greyish nodules, and at the upper pole was a bluish-red mass the size of a walnut. The tumor tissue was composed of cavernous spaces filled with blood, and of cellular areas whose origin could be traced to the endothelium of the sinuses. Because some of the greyish nodules contained an overgrowth of spindle-cell tissue, supposedly derived from the reticulum, the neoplasm was termed an angiomatous fibrosarcoma.

An unusual case in the older literature is that of Ramdohr,[82] also termed an angiosarcoma. This was a male infant who died within a few minutes after birth. The chin had been transformed into a large tumor into which hemorrhage had occurred. Other bluish-red nodules up to the size of a goose-egg were present in the skin of the abdomen, chest and upper and lower extremities, and similar nodules were present in both lungs and both kidneys. The tumors were composed of blood filled sinuses and cellular tissue made up of large polyhedral cells without supporting framework. A similarity to carcinoma was mentioned by the author.

A noteworthy example of vascular and endothelial tumor was reported by Shennan.[83] Although the patient, a woman, was 23 years old at the time of death, symptoms had been present for a number of years and the tumor was probably congenital in origin. At 17 years of age symptoms of mediastinal pressure developed, and from this time on the patient had repeated attacks of hemoptysis. Death occurred suddenly from mesenteric thrombosis. The mediastinum was filled by a mass of tissue composed of purplish cysts; similar tissue invaded the lung at its root and the capsular and subcapsular tissue of the liver. Microscopically the tumor in general was a cavernous hemangioma, with large, cystic blood spaces and well defined fibrous septa covered by endothelium. In places the latter was in active proliferation and formed cellular masses which were invasive. Metastasis to the lung and liver must have been due to such proliferating tissue. The striking feature is that the metastasizing endothelium retained its angioblastic potentialities and differentiated to form blood spaces in its new locations. Blahd, Maschke and Karsner[84] reported a hemangio-endothelioma of the ileum in a female child aged two months. At laparotomy for acute intestinal obstruction a constricting tumor was found 18 cm. above the ileo-cecal valve. Death followed the operation. The tumor tissue, present in the mesentery and in all the coats of the intestine except the submucosa, was composed of capillary blood-vessels, which were lined by prominent endothelium. In places the latter formed solid, cellular, alveolar areas, and showed evidence of invasion.

A new-growth which deserves particular mention because of its location and clinical manifestations was reported by Armstrong and Mönckeberg.[85] At the age of 5½ years a boy, who had just recovered from a short, acute illness of undetermined nature, began to have repeated syncopal attacks, with marked cyanosis and sometimes with loss of consciousness. These were apparently typical attacks of Stokes-Adams syndrome, during which the pulse could not be felt at the wrist. Repeated examinations in the course of a year, during which there were frequent attacks of syncope, showed a persistently low radial pulse rate. Pulse wave records revealed a condition of heart block with a ratio of auricular to ventricular rate which varied from 2 to 1 to 11 to 8. Death occurred 12 months after the first syncopal attack in such a seizure. The heart was normal on gross examination. Upon serial sectioning of the upper part of the ventricular septum there was found a poorly defined nodule of tumor tissue 8 by 6 by 5 mm., which occupied the region of the auriculo-ventricular node of the conduction system. The anterior division of the node was recognizable but was partly infiltrated. The posterior division and the immediately adjacent auricular muscle had been replaced by tumor tissue. The latter consisted of endothelial lined lymph spaces of somewhat variable size. The endothelium was proliferated, forming two to several layers of cells and in places completely filling the vessels (Fig. 335). The cells invaded the loose connective tissue stroma of the tumor. Mönckeberg considered the neoplasm a malignant, invasive lymphendothelioma, derived from the lymphatics of the conduction system.

In two endothelioblastomas of the penis, reported by Creite[86] and by Gobbi,[87] the derivation of the tumor cells from endothelium was less certainly established than in the above cases. Creite's patient was 26 months old. The penis was three times larger than normal and was constantly erect. Death from recurrence and metastasis occurred two months after amputation of the penis. The corpora cavernosa and the corpus spongiosum were occupied by cellular, alveolar tissue, which the author considered carcinoma, but which Schultze held to be endothelioma. Gobbi's patient was 10 months old. The penis was enlarged and erect. Metastases were present in the inguinal nodes. The condition was considered inoperable; death occurred 90 days after the onset of the first manifestations. The corpora cavernosa were occupied by a cellular, invasive endothelioma. In both of these cases the tumor probably arose from the endothelium of the sinuses of the corpus cavernosum.

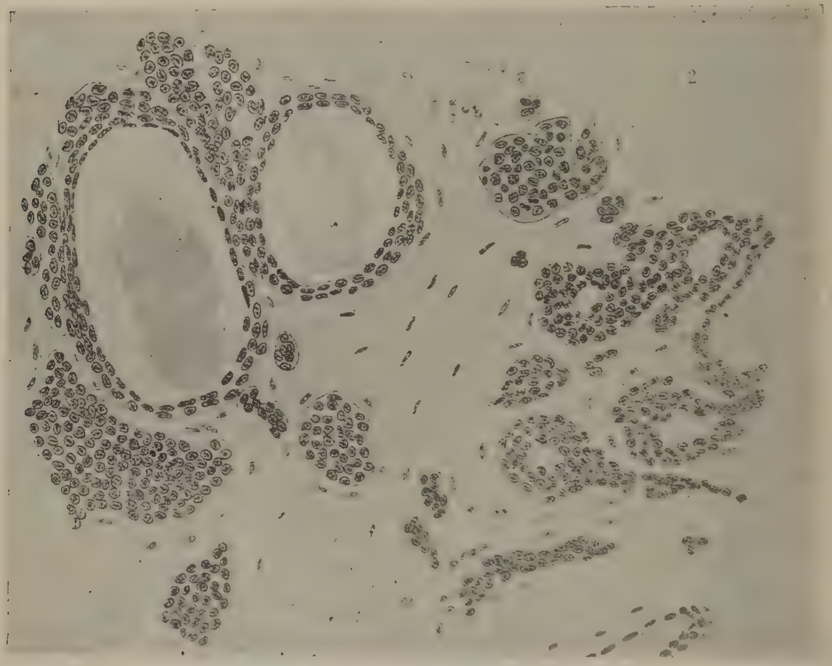
FIG. 335.—Lymphendothelioblastoma of conduction system of heart; boy aged 5½ years. (Armstrong and Mönckeberg.[85])

Serous Membrane Tumors.—In the controversial field of the endothelial tumors, probably most argument has been waged over the nature and position of certain tumors of the serous membranes, especially the pleura. Those who have held them to be endothelial in origin have disputed with each other as to whether the tumors arise from the covering cells of the serous membrane or from the true lymphatics beneath the surface. Those who have believed that the tumors arise from the covering cells have, in turn, disputed with each other as to whether the neoplasm is an endothelioma or a carcinoma. In favor of the latter was the older view that the lining of the serous cavities is derived from the celomic epithelium. The establishment of the origin of the serosal lining cells, like the endothelium of blood and lymph vessels, from the mesoblast indicated a close relationship of the two types of cells. In spite of this relationship, there are many who believe that the serosal lining cells, because of their epithelial character, constitute a special type of tissue for which the name mesothelium has been proposed. The serous membrane tumors, which occur most often in the pleura, may have a marked similarity to true carcinoma, hence the name *Endothelkrebs* of the German literature. This group of neoplasms has recently been subjected to critical analysis by Robertston,[88] who concluded that most of the reported examples have probably been true carcinomas. Upon the basis of cases studied by himself he removed them as a ground for contention as to their origin by concluding that they are not primary serous membrane tumors at all, but are secondary to primary epithelial neoplasms situated elsewhere, usually in the lung. It will remain for careful examination of future tumors of this kind to determine this point. There seems to be no logical reason why primary tumors derived from serosal lining cells should not occur.

v. Hibler[89] reported as a primary endothelial cancer of the pleura a tumor of a boy aged 5½ years. The entire right pleura had been transformed into a thick layer of dense, white neoplasm, with a nodular area the size of a fist. The tissue consisted of dense fibrous stroma in which were embedded solid cell nests and spaces lined by a single layer of cells. Other alveoli showed transitions from the single layered to the multilayered, solid condition. The tumor cells were described as being epithelial in their morphology. From a boy aged 15 years, with symptoms of brain tumor, Taylor[90] removed a tumor which had eroded through the squamous portion of the temporal bone. It arose in the dura and had not invaded the pia or the brain. Embedded in dense stroma was more cellular tissue which was composed of cells arranged in rows which followed a racemose course. The microscopic diagnosis was endothelioma of the dura. Recurrence, which was evident six weeks after operation, led to death. Nonne, according to Ford and Firor,[91] reported a case of meningeal tumor in a girl aged 16 years. The symptoms were those of brain tumor. The pia over the base of the brain, and to a lesser degree that over the convexity, was diffusely infiltrated by tumor tissue. The pia over the posterior surface of the cord was also thickened. Microscopically the thickened meninges were composed of oval and small spindle cells with relatively large nuclei. Nonne called the tumor an endothelioma. Ford and Firor believed that it probably belonged among the diffuse glioblastomas of the meninges.

Perithelioma.—Perithelioma has become a collective term for tumors whose only common feature is an intimate relationship of tumor cells to blood vessels. For one writer a perithelioma may be simply a vascular sarcoma in which necrosis has led to disappearance of tumor tissue except immediately about the vessels. For another, perithelioma may be a neoplasm in which new-formed blood-vessels are surrounded by thick mantles of sarcoma cells, presumably derived from the supporting tissue of the vascular adventitia; this is the perithelial hemangiosarcoma considered above under the sarcomas. For still another, perithelioma may be a tumor with a rich network of small vessels, upon which lie relatively large polygonal cells, often indistinctly subdivided into alveoli by the vascular network. It is for the latter type of neoplasm, presumably derived from perithelium, that the term perithelioma should be reserved. Ribbert[64] believed perithelium to be a layer of flattened cells applied to the outer surface of the wall of the blood-vessels of certain tissues. Others have held perithelium to be the endothelium of perivascular lymph spaces. For many, the existence of perithelium has not been established. Ribbert claimed that in no tumor reported as perithelioma had an origin from perithelial cells been proven.

Pes[92] described a perithelioma of the lachrymal gland in a girl aged 7½ months. The tumor had caused protrusion of the eyelid, a symptom which had been present for four months. In the center of the enlarged lachrymal gland was an angiomatous plexus. Clear, polyhedral cells were present on the walls of the vessels and filled in the spaces of the vascular network. Füth, according to Mönckeberg,[93] reported as a perithelioma a tumor of the jaw present in a new-born infant. The neoplasm was as large as a hen's egg and was of firm consistency. It was made up of rather large cells, subdivided into irregular, solid alveoli by a connective tissue network which carried small blood-vessels. The tumor also contained islands of epithelial cells, which were believed to have been derived from the enamel organ. It is possible that the entire tumor may have been an embryonic odontoma. Komocki[94] described a perithelioma of the pia of a girl aged 15 years. The tumor was situated between the cerebellum and medulla, and was composed of elongated cells which were arranged radially about thin walled blood-vessels and were supported by a finely fibrillated network. The description suggests a perivascular sarcoma rather than a true perithelioma.

Tumors arising from the carotid and coccygeal bodies have also been named peritheliomas. The only reason for applying this name to such neoplasms is their morphologic similarity to those tumors which are believed to come from true perithelium. The tumor cells fill in the meshes of a thin walled, vascular network. Mönckeberg[95] and others have shown that the cells give the chrome reaction of the parasympathetic system, from which the carotid and coccygeal bodies are derived. The cells of these so-called peritheliomas must come, therefore, from the parenchyma of these bodies, and not from perithelium. The mosaic arrangement of the tissue of hypernephromas has led some writers to place these tumors also in the perithelioma group.

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CHAPTER CXCIV

ENCEPHALITIS

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I. Non-suppurative Encephalitis.
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  9. Prognosis.

NON-SUPPURATIVE ENCEPHALITIS ("STRÜMPELL-MARIE" ENCEPHALITIS, "STRÜMPELL-LEICHTENSTERN" ENCEPHALITIS)

Introduction.—Due to the wide discrepancy between clinical manifestations and pathological background, the disease known as *non-suppurative encephalitis* has remained a complicated and somewhat chaotic field of childhood neurology. Its history and study have been intimately connected with the so-called "cerebral palsies of children," and because of the fact that practically all of the autopsy material becomes available years after the acute illness, it became difficult to decide whether the late findings of softening, sclerosis, and large cavities were to be traced back to a toxic-infectious origin, or whether they were dependent on mechanical vascular injury and occlusion, or on a primary developmental defect.

A brief historical introduction will help to make clear the complexity which besets the problem. In 1827 Cazauvielh[6] published a study upon cerebral agenesia and congenital paralysis which is the real beginning of the modern study of the diseased picture. He described a one-sided paralysis with hypertonia and contracture and mental deficiency. In his pathological studies he found one group of his cases with what he regarded as a primary developmental defect of one hemisphere without lesion of the supporting tissue which he called "Agenesie Primitive," and in the rest of his material he found in addition to the reduction of the size of the hemisphere alterations in the supporting tissue—*i.e.* (cysts and softening). This he regarded as an agenesis of secondary origin due to unknown, but definite pathological processes. At nearly the same time Dugés[10] proposed the idea that these alterations were due to a prenatal encephalitis.

About 1850 came Virchow's epoch-making studies on thrombosis and embolism which led the way to the understanding of a number of the cases. He admitted, in addition to those cases due to mere mechanical blocking, the non-mechanical origin of certain of the cases and suggested that an irritative (inflammatory) process was responsible for many cases. He further described a congenital interstitial encephalitis; which he held to be inflammatory. In 1868 Cotard[8] under the direction of Charcot, undertook a study of the pathological alterations of childhood brain atrophy. He emphasized diseased foci rather than atrophy, and described four pathological conditions: *First,* yellow plaques; *second,* cysts and cell infiltration; *third,* a loss of substance with resorption of the diseased nervous tissue; and, *fourth,* the alterations of diffuse lobar sclerosis. He regarded the first two as primary lesions, and the sclerosis as secondary to the primary alterations. The primitive lesions he regarded as due to softening, apoplexy, meningeal hemorrhage, traumatic encephalitis, and primary cortical sclerosis. Hayem's[18] pathological studies of 1868 gave the first well rounded evidence of a non-suppurative encephalitis—according to his description a "hyperplastic encephalitis." In the same year Heschl[19] made a special study of the cases which showed substance loss with cavity formation which he called porencephaly. Leyden[24] (1876) described the first authentic case of bulbar paralysis clearly showing focal disease of the medulla. In 1881 came Wernicke's[58] important studies on acute hemorrhagic polioencephalitis, superior of alcoholic etiology. Richardiere[47] (1885) saw in lobar sclerosis the explanation of all of this childhood paralysis. In 1885 Jendrassik and Marie[21] were able to shed some light on the origin of this cerebral sclerosis suggesting that the sclerotic alterations began in the perivascular spaces and in the vessel walls. They proposed the notion that the sclerosis might affect the surrounding brain area or the whole hemisphere directly without vascular disease and emphasized the occurrence of the paralysis during the course of acute infectious diseases. Little,[25] in 1862, and Sarah McNutt,[31] in 1885, established the role of brain injuries and meningeal hemorrhage as a definite etiology for a definite group of early cerebral palsies. Benedict,[31] in 1868, distinguished the post-hemiplegic chorea from idiopathic chorea, and in 1868 Hughlings Jackson described cases with one-sided convulsions. In 1884 the whole problem was given a tremendous impetus by Strümpell.[52] He suggested that just as poliomyelitis affected the anterior horn cells, just so the gray substance of the cerebral cortex might be affected by the same disease which he called polioencephalitis.

Strümpell's[52] proposal was immediately met by ardent supporters and opponents. P. Marie,[28] the following year, supported his view but emphasized the fact that the poliomyelitis virus was responsible for only a certain group of cases, and that the sequence of the acute infectious diseases and encephalitis was too frequent to be merely of casual importance. He was able in support of the position of Strümpell,[52] to rediscover two cases of Möbius[32]—two children of the same family, one with typical spinal involvement and the other with a hemiplegia of cerebral origin. On the pathological side he held to his notion of primary vascular involvement and denied the purely cortical nature of the disease. So important had these two contributions been to the study of encephalitis that the disease is frequently known as "Strümpell Marie disease." Strümpell[52] later modified his views admitting that the disease affected the white matter as well as the gray, and he no longer held that the poliomyelitis virus was the sole etiology. Then followed a series of excellent clinical studies—Osler,[41] in 1888, and in the same year Lovett,[26] Sachs and Peterson[48] in 1890, and in 1891 the very excellent clinical study of Freud and Rie.[13]. Osler[41] was inclined to give more weight to the Strümpell[52] position, but Freud while not denying the validity of the proposal, held that evidence from a pathological point of view was lacking.

1892 brought Leichtenstern's[22] observations on the occurrence of the disease during influenza epidemics and the view that the influenza bacillus or toxin might be responsible for many cases. Although the absence of bacteriologic findings threw doubt on this view, yet sufficient evidence has subsequently come forth in its support so that Leichtenstern's[22] name is coupled with the disease, especially in Germany. Later Southard and Keen[51] were able to cultivate streptococci and other organisms from the cerebral lesions and questioned whether these were primary or secondary invaders.

Oppenheim[39] gave a series of valuable studies from 1887 to 1901, emphasizing first, the pathological findings (hemorrhagic foci, varying from microscopic to large areas, round cell infiltration, the multifarious localization of the process and the direct influence of toxins on the nerve cells), and second, the not infrequent benign course of all forms. In 1907 followed his very complete monograph on encephalitis.[40] We find then gradual evolvement of a disease picture which presents manifold cerebral localization, either the result of a specific infectious disease, or following non-specific acute infections. The end result is a chronic nervous disorder, with cerebral softening, atrophy, sclerosis, or porencephaly.

Etiology, Age, Sex, Previous Condition of Health.—(*A*) Primary infections stand at the head of the list of causal agents. According to Taylor[7] at least one-third of the cases definitely have an infectious etiology. It is conceded by most observers that the disease may occur as an independent infection, whether one admits that it is related to poliomyelitis or not. There is now considerable evidence, both clinical and pathological, that the disease occurs during epidemics of poliomyelitis, but that it also presents as an acute infection without recognizable etiology, although Taylor[53] and Oppenheim[39] regard a mycotic origin as certain. A number of observers have found various organisms in the brain, streptococci, staphylococci (Southard and Keen)[51] and mixed staphylococci and streptococci, Reymond's[46] case. Finkelstein[12] describes a septic form, dependent upon a blood stream infection, usually streptococci. Further Oppenheim[39] believes it may occur as an abortive form of epidemic meningitis.

(*B*) Secondary to Other Infectious Disease.—Marie's[28] original contention that the disease is etiologically connected with the acute infectious diseases now seems to be clearly established clinically. Whether this is due to direct bacterial invasion or is due to toxins is not clear, although the latter view has much to support it. The disease most frequently follows scarlet fever and measles but the list includes almost all the acute infections.

The following is a fairly complete list: Scarlet fever, Osler,[41] Freud,[13] Gowers;[16] measles, Bernhardt;[4] mumps, Mayrhofer-Grünbühel;[30] dysentery, Lenhartz;[23] chicken-pox, Taylor;[53] pneumonia, Finkelstein;[12] typhoid fever, Osler;[41] influenza, Pfuhl,[42] Nawwerk;[36] otitis media, Oppenheim;[39] Septicemia, Muratow;[35] typhus, Oppenheim;[39] chorea; Oppenheim;[39] diphtheria, Seifert;[49] small-pox, Freud;[13] epidemic meningitis, Leichtenstern;[22] german measles, Taylor;[53] vaccination, Osler, [41] Marie;[28] sepsis, Seitz,[50] Finkelstein;[12] syphilis, Oppenheim;[39] acute rheumatic fever, Freud;[13] tuberculosis, Nonne.[37] The disease may occur at any stage of the infections and may not appear until convalescence is well established.

The role of trauma is still much in doubt. It is true that a very slight injury to the head, either a fall or a blow, may precipitate or just precede the first sign of an attack. It is questionable whether the injury merely calls attention to, or precipitates the illness, or whether the brain injury forms a nidus for infection. It has been maintained especially by the older observers that it may alone be adequate cause (sui generis).

Even more obscurity surrounds fright as a causative agent. Clear cut cases of hemiplegia, with or without chorea, have been reported with a complete absence of other etiologic factors. No doubt a number of cases are hysterical but there exists cases in which the latter explanation can not hold.

Toxins and poisons of a non-bacterial origin undoubtedly produce an acute hemorrhagic encephalitis. Fish and food poisoning (meat, sausage); gasoline, Pott's;[43] salvarsan, Rasch;[44] lysol, Oppenheim;[39] alcohol, Wernicke;[58] have been described. They are apt to produce special forms of the disease with localization in the grey matter of the aqueduct of Sylvius.

Age, Sex, Previous Condition of Health.—The disease is essentially one of early childhood and most of the cases occur before the third year of life. Two-thirds of Freud's[13] series occurred during the first three years of life—and the series of Osler,[41] Wallenberg,[57] Sachs and Peterson[48] verify this conclusively. After six years of age the disease is uncommon but cases have been reported at every period of life. Oppenheim[39] and Finkelstein[12] are agreed that the disease can occur prenatally and at the time of birth. Undoubtedly maternal infections are responsible for these intra-uterine forms. The disease affects males and females equally. Osler[41] has pointed out the fact that it usually attacks children who have been in excellent health up to the time of the attack.

Symptomatology and Course.—The symptomatology of the disease divides itself into three groups: (1) The initial or general symptoms, (2) focal symptoms, (3) late or residual symptoms.

1. The onset is usually acute. The child frequently complains of headache, loses appetite, is apathetic and inactive. There is usually fever which may be very high, 105–106 degrees, but may be very slight or completely absent. Nausea is present and usually vomiting. The condition may be ushered in by convulsions, or they may occur shortly after onset. They may be major with tonic and clonic movements or may be merely tonic. Only petit mal attacks may be observed. It is not uncommon to have only one-sided convulsions, and these without loss of consciousness. Along with these manifestations, the child is often stuporous, or confused and delirious. All of these initial symptoms may persist only a short time (one day) or may go on for many days or weeks. Usually they have disappeared by the second week. There may also be symptoms strongly suggesting a meningitis with opisthotonos and neck rigidity. Pupillary disturbances, however, are rare, Oppenheim.[38]

2. Usually at the height of the disease (on the second or third day, though sometimes at the onset, or late in convalescence) the focal symptoms appear. The character of these symptoms depends upon the localization of the process. In the great majority of cases the focal symptom is hemiplegia. If unilateral convulsions have initiated the attacks it is usually this side which shows the paralysis. At first the hemiplegia is flaccid, but very shortly shows signs of rigidity or spasticity. The arm is usually more severely involved than the leg. The face may or may not participate in the weakness or paralysis. The hemiplegia may involve either side of the body and in some cases both sides are involved in a bilateral hemiplegia. Monoplegias can occur, and diplegias as well as paraplegias, although there is much evidence that paraplegic and diplegic forms usually are due to developmental malformation of a non-encephalitic character, or to birth trauma.

If the process involve the speech areas aphasia accompanies the picture. This may occur either with a right or left hemiplegia. Apparently the child's brain does not acquire its definite one-sided primary localization of speech until a later date. The aphasia may be shown in definite paraphasic disturbance, or there may be merely a general word reduction. If the occipital, especially the calcarine cortex be involved a hemianopsia results (Freud,[13] personal observation).

With a very wide spread process complete deafness and mutism can result. If, instead of a primary cerebral localization the process involves the cerebellum, it produces the symptoms of ataxia, unsteadiness of movement, over-reaching, etc. and nystagmus. When the region of the aqueduct of Sylvius is involved one sees eye muscle involvement, strabismus, paralysis of various eye muscles, although conjugate deviation of the eyes may be due to cerebral involvement. There may also be somnalence due to involvement in this region, Oppenheim.[39]

The primary invasion may effect the bulb either in the region of the sixth, seventh, and eighth nerves or still further down and we then have various cranial nerves involved with facial paralysis, difficulty in swallowing, deviation of tongue, dysarthria, internal strabismus, or nystagmus (vestibular).

We may have practically every portion of the brain involved in one case or the other, although, as has been stated above, the cerebrum is the usual seat of the process and the vast majority of cases present hemiplegia. Disturbances of sensation are rare but if the internal capsule is involved in the thalamus we may have hemianalgesia and general reduction of sensibility in the affected side. These disturbances are usually transitory.

Death or recovery may occur at any time during these first two stages of the disease. If death does not supervene the recovery may go on to complete healing. This is not rare, according to Oppenheim's[39] experience. If recovery is not complete, however, the third stage of the symptoms is seen.

3. Final Stage with Residual Symptoms.—Even if the condition does not go on to complete recovery, one may expect to find a definite amount of improvement. In the hemiplegic forms the leg first shows improvement, then the face, and finally the arm. The disturbance disappears, or improves first in the proximal portions of the limbs, and only later, if at all, in the distal joints. The fingers are apt to show the least improvement. It is remarkable how much function can be retained in a very severely paralyzed member. The picture usually presents an increasing degree of rigidity and then contracture as the permanent stage of the illness is reached. The gait, while the leg is affected, shows the typical hemiplegic circumduction in walking, and while standing the child is apt to have the knee somewhat flexed and the foot in the position of talipes equinovarus. The arm is flexed, held close to the body, and the wrist is in semi-pronation, with the fingers bent into the palm of the hand, enclosing the thumb which is drawn over the palm of the hand. The facial palsies are very common, occurring in two-thirds of the cases, (Freud[13]) and are more apparent on mimetic movements than when the movements are voluntarily innervated. The lid slit, (Sachs and Peterson[48]) is usually wider on the

paralyzed side. With the development of the rigidity and contracture, there is a general atrophy of the affected limb with atrophy and apparent shortening of the long bones. The degree of atrophy is in large measure determined by the degree of paresis of the member. Freud[13] is inclined to doubt this relationship. Along with the general atrophy of the extremities there may be similar change in the cranium, face, chest, and buttocks. The cranial bones show flattening and thinning, the face shows a hemiatrophy, the mamma is small, and the chest wall is of smaller girth on the side of the hemiplegia.

The trophic changes are very striking. The paralyzed limb is cooler than the normal side; and its color is a livid red blue. The atrophy may be masked by a fatty hypertrophy. This is more apt to occur when perverse movements have been superimposed.

The perverse movements that appear, are among the most distressing of all the symptoms. These movements may be grouped as those[1] occurring on voluntary effort and[2] those appearing spontaneously. The voluntary group includes increased spasticity, tremor, ataxia, chorea, and associated movements; the involuntary group includes athetosis and epileptiform myoclonus (Taylor[53]). The increased tonus or spasticity usually develops shortly after the paralytic symptom appears and show steady progression. The degree of spasticity is increased by voluntary activity. It is a great hindrance to activity and may be so profound that it simulates a much greater degree of paralysis than actually exists. Although spasticity does not exclude the occurrence of choreatic manifestation yet on the whole the two rarely occur together. The chorea usually appears as the spasticity begins to recede, although it may be present from the beginning even in the presence of a mild degree of spasticity (Freud[13]). The chorea is usually a hemichorea and has all the characteristics of the Sydenham's chorea. It may, however, be bilateral if the hemiplegia is bilateral. The face, tongue, and eyes may be involved, and both upper and lower extremities. Cases are seen in which the movements are limited to the face or either of the extremities. Freud[13] summarizes the time relations of chorea to spastic paralysis as follows:

First.—It may appear in place of paralysis as a primary chorea in both extremities (choreatic paresis).

Second.—It may appear as a primary chorea of one of the extremities while the other is spastically paralyzed (transition form).

Third.—The chorea may appear after the spastic paralysis has regressed and this may happen (*a*) to both or (*b*) to only one extremity.

Fourth.—There may appear side by side chorea and spastic paralysis. One may, therefore, speak of early and late chorea. The ataxia manifests itself as a clumsiness of movement, over-reaching, uncertainty, and falling. Tremor of every variety may exist from coarse to fine tremor, spontaneous, and intention tremor. This symptom is usually a transitory one.

Rarely, associated movements, Sachs and Peterson,[48] are observed in the paralyzed side. With every movement of the normal side, there is a tendency to either repeat the movement on the affected side or to start some perverse movement.

The most frequent perverse movements which occur spontaneously are known as athetosis. The distinction between chorea and athetosis can not be sharply drawn, although the athetoid movements are as a rule, much slower, more rhythmic, and less purposeful than the choreatic ones. There are, however, transition forms which it is impossible to put clearly into one class or another, Freud.[13] Unlike chorea, the athetosis may occur in very spastic extremities and may give rise to great hypertrophy due to the incessant movements of the affected limb.

Unfortunately, in addition to the motor disturbances, a large proportion of these children have a definite reduction in mental capacity, due to the wide-spread cortical injury. From the time of the illness on the child may never show any evidence of further mental development or may begin to have signs of distinct retardation. In some cases all the previous mental development is lost and the child regresses to a level of complete absence of all mental capacity. We may see every stage of mental defect. In Sach's and Peterson's[48] series over one-half of the cases showed mental defect. In our own experience the percentage is higher.

What makes the disease a still more ominous one is the great frequency with which epilepsy follows upon it. This may first make its appearance, Freud,[13] years after the conclusion of the acute disease process although it usually appears sooner. The attacks may be Jacksonian in type, or may be generalized convulsions. Not infrequently only petit mal may occur for a long time before the major convulsions appear or the latter may never occur. Epilepsy is usually progressive and increasingly severe with accompanying mental deterioration.

Pathological Anatomy.—The pathological study of acute-non-suppurative encephalitis offers difficulty because of the comparative rarity of material. The great majority of autopsies have been done on cases of long standing, and it is, therefore, difficult to trace back the sequence of events from the acute encephalitis to the end results or even be sure that the original disease was an encephalitis. The best description of the acute cases is that of Oppenheim.[39] The process is primarily an acute inflammatory one with hemorrhagic manifestations. It is usually limited to a circumscribed area and not infrequently involves symmetrical parts of the brain. It may affect either the cortex, the subjacent white matter, the basal ganglia, the midbrain, hindbrain (medulla oblongata), or cerebellum.

Macroscopically one finds the affected areas hyperemic and usually somewhat swollen and softer than normal. The pia overlying the affected cortex may be hyperemic and even slightly clouded if any meningitis accompanies the process.

On section or on the surface of the cortex one often sees, usually macroscopically, and always on microscopic examination, numerous small punctuate hemorrhages for which Oppenheim[39] suggests the term "flea bitten" appearance. The hemorrhages may be pin point in size or large and confluent hemorrhages, so large as to suggest the rupture of a vessel as a primary cause of the disturbance. The small arteries and capillaries are the first involved and show great widening. They are engorged with red blood cells and these latter are also found in the blood vessel walls. Probably this is explained by diapedesis due to slowing of the blood stream, but it may in addition be caused by the actual rupture of the vessel wall, in which case the blood is found in the surrounding tissue spaces. If larger vessels are involved one gets, of course, large hemorrhages. In addition, the smaller vessels show marked perivascular lymph-space infiltration with round cells, including lymphocytes, plasma cells, and polyblasts. While the majority of investigators hold to the view that the arteries are the primary seat of the inflammatory process there are others who feel that the primary affection is on the venous side. Although the evidence is scanty this hypothesis would explain somewhat more easily the development of the more chronic forms, without dissolution of brain tissue. Still others, Taylor,[53] however, think that the process involves all of the elements of the central nervous system simultaneously.

What has been described above may be said to constitute the initial or potentially reparable stage of the process. It is clear that, inasmuch as cases may go to complete recovery from this point, that the process may start healing from this time on. Oppenheim,[39] who saw a case at operation with this much damage, was able some time later when death occurred from some other disease, to examine the process of healing. He found areas of scarring in the white matter and in the cortex but with no impairment of the ganglion cells.

If the process continues further thrombi are found in the vessels, and areas of small or large softening, according to the size of the vessel involved. Freud[13] reports one case from Charcot's laboratory in which the sclerotic area followed accurately the distribution of the anterior cerebral and the sphenoidal branch of the middle cerebral artery. With partial or complete occlusion of an artery one of several sequellæ may be expected. (1) The softening may go on to cavity formation and if a large area is involved may ultimately result in porencephaly, which may or may not communicate with the ventricle, or (2) if the area is smaller we may get cyst formation (it is apparently possible for cysts to develop with great rapidity—in 21 days in one of Taylor's[53] cases), or (3) if the areas are small we may get scarring. By some observers led by Abercrombie[1] the cause of the arterial blockage is attributed to embolism. This is supported in part by the occurrence of the disease with scarlatinal endocarditis and with whooping cough, but the review of the autopsy material by Osler[41] showed *surprisingly* few cases with this etiology. Taylor[53] has pointed out that in childhood "the result of vascular blocking is peculiar. Atrophy without death of the supporting tissue is the rule and avascularized convolutions, still retaining their form and color, shrink and become hard, and the sulci are widened. Microscopically the nerve elements are gone and the glia increased. Sometimes complete absorption may be so exactly limited that excavation takes place." This then in the first instance will result in cerebral sclerosis or atrophy, and in the latter in porencephaly. It is the attempt to explain the atrophic and sclerotic changes—that is, the persistence of the supporting elements and the disappearance of the nervous elements that lead to the venous hypothesis, Gowers.[16] Persistent venous blockage or stasis would lead to ganglion cell asphyxia and to the retention of the more resistant element of the tissue—the glia. Only rarely, however, has any autopsy material supported this latter view. The sclerosis is held by many to be the result of hypertrophy of the glial elements.

It has been doubted by many whether porencephaly and cerebral sclerosis have any relation to acute encephalitis, but the majority of the best observers admit the possibility, Oppenheim,[39] Freud,[13] Finkelstein.[12]

It is further to be noted that encephalitis occurs along with varying degrees of meningeal irritation and has been observed surrounding areas of abscess formation, Oppenheim.[39] The meningeal form is particularly important because it may give rise to all the symptoms of tumor when it appears as a meningitis serosa, Nonne.[37]

The bacteriological studies of the brain tissue has led to very conflicting results. Streptococci, staphlococci, influenza bacilli, and mixed infections have been found, Southard and Keen,[51] Seitz,[50] etc. Blastomycosis has also been described, Türk.[55] The great majority of cases, however, show no organism—at least none that can be cultivated by the present methods. Taylor[53] believes that all cases are due to micro-organisms as yet unidentified.

Diagnosis and Differential Diagnosis.—The diagnosis in typical cases may be very simple especially when it presents during the early years of life with fever, vomiting, and convulsions, when focal symptoms such as hemiplegia occur early in the disease or when the focal symptoms follow an acute infectious disease. However, the diagnosis should always be made with a deal of reservation because of the great variety of conditions which are easily confused with it. This is especially true when the condition has to be diagnosed in retrospect, i.e., after the acute attack is over. It is important to bear in mind that the absence of the triad, fever, vomiting, or convulsions does not exclude the diagnosis nor is an acute onset necessary.

The differential diagnosis must be made with the following conditions: (1) Cerebral hemorrhage, (2) thrombosis, (3) embolism, (4) meningitis, (5) acute infectious diseases with convulsions at onset, (6) brain abscess, (7) sinus thrombosis, (8) meningitis serosa, (9) poliomyelitis, (10) paralyses of spinal origin, (11) cerebral palsies due to birth injury, (12) cerebral palsies due to cortical agnesia, (13) brain tumor.

1, 2, 3. A diagnosis of *hemorrhage*, *thrombosis*, or *embolism* of one of the cerebral arteries in childhood is very difficult. It is important to realize that it is a rare condition. It does occur, especially in luetic children, but very often is secondary to an encephalitis. The differential diagnosis with encephalitis can rarely be made. The absence of fever with a delay in the occurrence of focal signs is somewhat in favor of encephalitis but most frequently the diagnosis can only be made at necropsy.

4. From *acute meningitis* the distinguishing features are the absence of retraction of head, and Kernig's sign, the rigidity of the pupils and strabismus, as well as the difference in spinal fluid findings. It is to be born in mind, however, that all these symptoms may occur in encephalitis.

5. The fact that *infectious diseases* are so often ushered in with convulsions and vomiting may leave one in doubt for a time whether the condition is not one of encephalitis. The absence of focal signs and the development of positive symptoms of the individual infectious diseases make this differentiation simple.

6. *Brain Abscess.*—History of local disease of the ears or bones of the nose or history of fracture and injury, the presence of increased intracranial pressure, with optic papilledema or neuritis, separate the condition from encephalitis but it may be impossible to make the diagnosis.

7. *Sinus Thrombosis.*—The presence of high fever of an intermitting character, external evidence or venous stasis, or chronic ear disease and mastoiditis, will serve as differentiating features when they are present but, unfortunately, these signs are so often absent that a certain diagnosis is frequently not possible.

8. *Meningitis Serosa.*—A serous meningitis often accompanies an encephalitis and may give rise to symptoms suggesting tumor. The gradual subsidence of the choked disc and the general improvement with reduction of the increased intracranial pressure either spontaneously or after decompression gives a late clue to the real condition.

9. *Poliomyelitis.*—If poliomyelitis affects only one side of the body or is bulbar in distribution only a careful study of the type of paralysis makes the diagnosis. The reaction of degeneration is, of course, present in the spinal types and not in the cerebral. Sufficient observations are now on record to show that poliomyelitis may be a polioencephalomyelitis as well. The occurrence of encephalitis during an epidemic of poliomyelitis should make one suspect the real character of the disease.

10. *Paralyses due to spinal origin* are to be distinguished by the absence of deep reflexes, the presence of reaction of degeneration, the lack of rigidity and spasticity.

11. The *palsies due to birth injuries* can only cause confusion if one sees the case long after the injury or if the paralyses first become apparent at a later stage of the child's development or during the course of an acute infection. The birth palsies are more apt to be diplegias or paraplegias and spasticity is more marked than paralysis.

12. The *cerebral palsies* due to cerebral agenesia very often presents difficulties because the defect does not make itself apparent during the first few months of life and only later does the parent first become aware of the difficulty. The absence of acute symptoms and the bilateral character of the paresis give a lead but the definite diagnosis may be impossible.

13. *Brain Tumor.*—If the first symptoms of the tumor are convulsions followed by paralysis, the diagnosis becomes very difficult, although the presence of fever and absence of choking of the optic discs are always in favor of encephalitis.

Laboratory Findings.—The blood usually shows a moderate increase in the number of white blood cells—as high as 20,000 per cm. There may be a relative increase in the number of polymorphonuclear leucocytes. The urine often shows albumen and some casts, but in no greater degree than that accompanying any of the usual infectious diseases.

The spinal fluid is often under increased pressure, contains frequently an increase in protein content, and the cells are slightly increased in number although not greatly—10 to 20 cells per cm. The gold-sol curve may show some decolorizaton in the middle series of tubes, but is very often unchanged. In a great number of cases there is little or no abnormality noted in the spinal fluid. The electrical reactions of the muscles show no reaction of degeneration—an important differential diagnostic point to distinguish these cerebral palsies from spinal ones.

Treatment.—Unfortunately, treatment must be entirely symptomatic. During the initial stages of the disease convulsions should be handled with choral and morphia, because they may actually endanger life itself. Fever, if high, should indicate sponges. The water intake should be carefully watched, especially if the children are unconscious. One may have to use hypodermoclysis, or in long standing severe cases intravenous or intraperitoneal salt infusion.

After the acute stages are over the paralyzed limbs should receive careful attention, and in addition to regular massage, passive movements should be used. The child should be forced to use the affected limb and not be allowed to slight it. Later, systematic exercise and gymnastics should be begun. It is often surprising how much function can be obtained by long continued work along these lines.

Prognosis.—The outcome may be recovery from the acute infection with or without residual symptoms, or may result in death. There seems to be practically no relation between the severity of the initial symptoms and the outcome, although profound drowsiness and stupor are unfavorable. That the patients may recover without residual symptoms of any sort has been emphasized by Oppenheim.[39] For the cases that recover from the acute symptoms but are left with paralytic residuals, it is possible that within three to six months all the paralytic symptoms will disappear. On the other hand, although some improvement is the rule, the restitution may stop at any time.

It is further possible that after some days or months that a hemiplegia may develop into a paraplegia. The cases of mental defect are the least favorable and show the least improvement. The possibility of epilepsy should always be kept in mind because this may develop even years after the initial attack. The prognosis in the cases developing chorea and athetosis is distinctly unfavorable as far as this individual symptom is concerned. The aphasia is very often transient but it not infrequently happens that cases accompanied by mental defect will lose what speech has been learned and be reduced to a few simple words. In the younger children the development of speech is often permanently impaired or they may never learn to talk. It is probable that deaf mutism in some cases is due to an early encephalitis.

CONGENITAL INTERSTITIAL ENCEPHALITIS (VIRCHOW)

Virchow undertook the investigation of the basis of a certain group of stillborn children and children dying early in life from unknown causes and found, in the brains of these children, areas in which there was diffuse infiltration of fatty cells with divided nuclei, Körnchenzellen, as well as clumps of these cells in areas which were hyperemic. The areas affected were the subcortical white matter and the corpus callosum. He held the condition to be an acute interstitial encephalitis, due either to a toxic or infectious origin. These changes are not macroscopic and are only seen when they are examined microscopically. These areas tend to soften and ultimately to become typical macroscopic softenings. He thought that these fatty cells were changed glia cells. Jastrowitz[20] opposed Virchow's[56] view with the finding that from the fifth intrauterine month until the seventh or eighth extrauterine month, these fatty cells were a normal physiological finding, and were associated with the destructive products incident to myelinization. He did, however, admit that the formation of large collections of these cells was pathological. He further insisted that it should be viewed as pathological when it involved the grey substance, and when it was found beyond the eighth month.

Ceelen[7] in 1920 investigated a series of cases and found in six cases in which a diagnosis of tetanus neonatorum had been made but in which the bacteriologial investigation failed to discover the tetanus bacillus, that the brains showed typical collections of these fatty cell masses, usually found subependymally, together with small hemorrhages and round cell infiltration of the smaller blood vessels. In addition to these cases he studied the brains of full term infants who had died without demonstrable cause. He found a gradation of findings from those described above to the complete absence of any findings. This led him to believ that if these findings are responsible in some cases, certainly many cases of still birth (all his cases showed inflated lungs) are not to be accounted for by this type of encephalitis.

It is clear that as yet we have no correlation between the pathological findings of Virchow's[56] encephalitis and clinical pictures.

The evidence up to date would seem to point to two clinical conditions which have shown the described alterations: (1)Certain cases resembling tetanus of the new born, (2) certain stillborn children, who apparently were viable (lungs show expansion).

We append two cases, one from Ceelen, and one from Finkelstein, to illustrate these types. It must be recognized that the disease entity at present is not a definite one, but as Ceelen points out the findings can have important medico-legal aspects in relation to the question of viability and death before delivery.

Case 8.—(Ceelen[7]) Strong, 52 cm. long, child born dead at term. Examination showed small areas of atelectasis; thymus weight 14 gm.; no sign of syphilis. The brain showed innumerable foci of cell infiltrations, with punctiform hemorrhages, subependymally. The infiltrate was made up of medium large cells with fatty cells. The blood vessels were congested.

Case X.—(Finkelstein,[12] Textbook, 2nd Edition, page 485.) A four weeks old child, with gastric symptoms for three days. On fourth day fever, vomiting, restless, with twitchings in face. Double sided otitis media, but condition unchanged after paracentesis. The following day tetanus spasm of the entire musculature. Dead same evening. Autopsy showed unimportant gastroenteritis, and bronchopneumonia. Brain deeply injected, with masses of fatty cell infiltration everywhere. Blood and spinal fluid cultures negative.

ACUTE CEREBRAL ATAXIA

Under this designation has been included a small number of cases of ataxia without paralyses coming on after or during acute infectious disease. Unfortunately, little is known of the condition pathologically because only one or two cases have come to autopsy. A case described by Ebstein[11] showed no cerebral alterations but a sclerosis in the medulla, but the view is still held by many that the condition can arise from purely cerebral damage. This view, argues Lüthje,[27] is correct, because the manifestations of unconsciousness and delirium, the loss of speech and memory, etc., are essentially determined by forebrain lesions. It does not seem clear to the writer that in addition the cerebellum and vestibular apparatus, may not also be involved. The clinical picture summarized by Lüthje is as follows: Severe acute infection (in his case typhoid); unconsciousness of several weeks duration with occasional delirium; then after mental clearness, the appearance of severe ataxia in practically all muscle groups, without paralytic symptoms; no sensibility disturbance; slight disturbance of intelligence (memory loss); severe vasomotor excitability; monotone, syllabic speech; increased deep and superficial reflexes; cases also exist with symptoms of less severity. The cases tend to run a slow but benign course with final outcome in complete recovery, with only slight residual.

ENCEPHALITIS WITH APRAXIA AND COMPLETE MENTAL DETERIORATION (TERGAST[54])

Another rare form of encephalitis has been described by Tergast,[54] in which the child is taken acutely ill with convulsions and unconsciousness, but without fever. One sided symptoms appear early in which a definite apraxia is noted. Gradually the general condition improves but leaves the child with the apraxia and complete mental deterioration.

ACUTE SEROUS ENCEPHALITIS

Recently Broan and Symmers[5] have observed a new type of encephalitis which runs a very fulminative course and terminates in death. The age of the children varied for 22 months to 7 years. The illness begins acutely with irritability, loss of appetite, vomiting, fever, and then evidence of central nervous system involvement becomes apparent —ptosis, strabismus, nystagmus, chocked discs, disturbance of respiration, muscle twitchings, stiffness of neck, trismus, hemiplegia, coma, and convulsions. Death occurs in 36 hours to 5 days.

Pathologically, the cases show edema of the pia and arachnoid, blood vessels engorged, perivascular spaces edematous, and occasional small hemorrhage. The glia is swollen and the spaces about the glia cells are edematous. Occasionally they found collections of glia cell and of lymphocytes. In no case was any perivascular cell infiltration found as in poliomyelitis, or epidemic encephalitis.

ACUTE CEREBRAL TREMOR

A rare form of tremor of cerebral origin has been described which comes on after acute infections and runs a benign course, Griffith.[17] It usually occurs in infants from 6 to 18 months of age, and has been seen after measles, febrile gastro-intestinal disease, and whooping cough. About two to four weeks after the acute infection the child suddenly develops a coarse tremor of the one or both sides of the body, suggesting the tremor of Parkinson's disease. The head may also be involved with a coarse or fine tremor. The extremities are apt to show slight paresis, and ataxia, with some spasticity in the extremities. There may be opisthotonus, or rather forced backward position of the head, i.e., the child apparently chooses this position for the head. Fever is either absent or very low. The child is apt to be restless, and sleepless, and occasionally there is vomiting. Recovery takes place in 2 to 12 weeks without residuals.

Zappert[60] and Finkelstein[12] both regard the disease as an encephalitis of a toxic or infectious etiology. Zappert[60] has seen one case come after sausage poisoning. They are both inclined to regard it as a benign form of encephalitis which leads to death or paralyses in the more severe cases. Up to date no pathological findings have been reported because death does not occur.

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EPIDEMIC ENCEPHALITIS (ENCEPHALITIS LETHARGICA, V. ECONOMO'S DISEASE)

Introduction.—In April of 1917 v. Economo[14] reported to the Wiener Gesellschaft für Neurologie und Psychiatrie, a group of cases, characterized by lethargy, somnolence and ocular palsies which he had observed in the late part of 1916 and the early part of 1917. These he designated as "encephalitis lethargica" and recalled a disease which had flourished in Northern Italy in the 1890's—a disease which had attracted much lay interest under the name of "nona." No medical reports of this epidemic or the disease itself are available, but newspaper accounts showed that it flourished during a great epidemic of influenza and presented the picture of lethargy with delirium. He also quoted Camerarius[14] who, in 1712, reported an epidemic disease in Tübingen called "die Schlafkrankheit," which was characterized by sleepiness, nocturnal delirium, ptosis, and other ocular manifestations. v. Economo was inclined to identify the disease described by him with those of the earlier epidemics. Under the name of diffuse myeloencephalitis at about the same time or even earlier, Cruchet[8] described cases occurring in Northern France similar to those of v. Economo, but it was not until the winter of 1917 when the disease made its appearance in Paris, that Netter[43] was able to give it its first French description under the title of "encephalitis lethargica." Soon afterwards cases began to appear in Africa, Asia, Australia, England, and America. Although the first English studies mistook the disease for a form of botulism, Hall[21] and Harris,[24] and, Batten and Still[4] described it as an epidemic stupor, its identity with the encephalitis described by Economo and Netter was soon recognized. As soon as it was discovered that lethargy was not a universal concomitant of the disease, and when it was recalled that 50 per cent. of non-suppurative, non-epidemic encephalitides showed drowsiness, Oppenheim,[45] the name "epidemic encephalitis" was suggested by Wilson;[61] and under this name it has become most widely known and described. It was soon recognized that the disease had actually assumed epidemic proportions and reports began to almost flood the medical literature, describing the protean manifestations of the new disease, its epidemiology, and pathology. Within a year or two after the disease had made its first appearance it was realized that the after effects of the illness were quite as serious as the acute illness itself or even more so, and that its later symptomatology was as varied as that of the acute disease picture. This again called forth a mass of reports, so that now after eight years we have a reasonably clear clinical picture of this disease and of its protean manifestations, both early and late; but although much work has been done upon its etiology and epidemiology little of certain value is actually known in this field.

Etiology and Epidemiology.—Although v. Economo[14] observed his original cases of epidemic encephalitis, before the pandemic of influenza invaded Austria, in 1917 and 1918, yet, because it occurred at about the same time as the 1917 influenza pandemic, and because similar cases were reputed to have accompanied earlier epidemics of influenza, the opinion for a time held sway that this newly described disease might be related to, or be a form of influenza itself. Crookshank[7] in an early study (1918) concluded that the two diseases had occurred simultaneously in the last four great epidemics of influenza. The collected evidence, however, has been gradually turning to the view that probably the diseases are not really related; at least if they are in any way connected, it is only that similar unknown factors tend to the simultaneous dissemination of the two diseases. The fact that the first cases preceded the influenza epidemic; that rarely does one have a history of preceding influenza in the individual case; and that a careful examination of the records of cases of previous influenza epidemics show that an encephalitis of influenzal origin is extremely rare (Strümpell reports only two cases from the pandemic of 1884), provide presumptive evidence against the relationship of the two diseases.

It was next questioned whether the disease was not an unusual form of epidemic poliomyelitis. Wilson[61] in 1918, summarized the arguments against its relationship to poliomyelitis and concluded that the diseases were totally unrelated. His conclusions have been concurred in by practically all subsequent investigators. The arguments in favor of the separate indentity of the two diseases are summarized by him as follows: (1) Poliomyelitis has its greatest incidence in the summer months (June, July, and August) while epidemic encephalitis is most frequent in the winter months (December, January, and February). (2) Poliomyelitis affects children almost exclusively and epidemic encephalitis adults preponderatingly. (3) More than one member of the same family is rarely attacked by epidemic encephalitis and several cases in one family are not at all uncommon in poliomyelitis. (4) If this be a form of poliomyelitis all the cases are atypical. (5) Lethargy is very rare in poliomyelitis. (6) Meningeal signs are common in poliomyelitis and rare in epidemic encephalitis. (7) The lesions of poliomyelitis are less patchy and more intense, and hemorrhagic manifestations are rarer in epidemic encephalitis. Further, Amoss[1] has shown that the convalescent serum of epidemic encephalitis does not neutralize the virus of poliomyelitis, while the convalescent serum of poliomyelitis does neutralize poliomyelitis virus.

That the disease is an infectious one, has not been doubted. Its febrile course and its pathologic anatomy make this certain, but it is more than doubtful whether it is actually contagious. Contact infection is extremely rare. Of 10,000 cases reviewed by Roger,[51] only 174 gave a history of possible contagion and these were far from certain. Two years after the beginning of the epidemic Netter[43] could find only eight cases in France in which two members of a family had been involved. Not a single example of bed to bed infection in hospital, nor infection from patient to nurse or doctor, has been reported. The only evidence of the contagious character of the disease is that it tends to be prevalent in cities rather than in the country. Although it was thought in the earlier years of the knowledge of the disease that it was only an epidemic one, yet time has clearly demonstrated that it is probably also to be endemic as well. The original epidemic subsided in 1919 but the year of 1924 saw it again assuming epidemic proportions in England and a large number of cases were seen in the United States. It is still very prevalent here, and in England.

Although adults are probably more often affected than children, yet the balance is not great on this side. Neal,[42] in 100 cases observed by her, found that one-half of them were under 15 years. No age would seem to offer protection against the infection; cases have been reported from earliest infancy, Hoobler,[28] to old age. If there is any difference in incidence between the sexes, it is probably that males are more often affected than females, but on the whole, most of the large series of cases show fairly equal distribution.

Simultaneously with publication of v. Ecónomo's[14] clinical description came an announcement of v. Wiesner[60] that he had isolated a gram-positive coccus from a fatal case, and that this same coccus could be recovered from a monkey who had been directedly innoculated from the brain material of this same patient. On the other hand he contended that it was not a filtrable virus because the filtrates of the brain material would not produce the disease in monkeys. Dimitz[11] and Cohn and Lauber[6] confirmed the finding of the coccus but were unable to transmit it to animals. No further confirmations of this organism have been forthcoming, and although from time to time a number of different organisms have been reported none has been further confirmed.

However, in May 1919, Loewe and Strauss[38] announced that they had succeeded in infecting monkeys with nasal washings from a patient with epidemic encephalitis, and that they had also been able to produce the disease in monkeys with a filtrable virus. By November, 1919, they[38] reported that they had succeeded in innoculating rabbits and also in passing the virus back and forward in monkeys and rabbits; and furthermore they described a very minute globoid organism in cultures of this virus. Their virus was obtainable from the spinal fluid, nasal washings and scrapings, and the brain substance of acute cases. Although they found 50 per cent. of their rabbits immune to experimental infection, yet, so constantly were they able to pass the disease to this animal that they suggested rabbit innoculation as an actual diagnostic measure. This work has been confirmed by Thalheimer,[58] and by Levaditi and Harvier,[35] and although the latter were able to obtain a fixed virus, it was only after many failures and in only one case were they finally successful. McIntosh and Turnbull[40] succeeded in passing the disease to monkeys from one case, but according to Flexner,[16] with less than sufficient technical precaution. Doerr[12] who had been working with herpes encephalitis, reported three cases of successful innoculation of rabbits with human encephalitic virus. Amoss and Flexner,[16] at the Rockefeller Institute, tried for three years to confirm these findings but were completely unsuccessful. Further, McCartney[16] investigated a series of 300 stock rabbits killed from other causes than encephalitis experimentation and found that 50 per cent. of the rabbits showed lesions in the brain identical with, or closely resembling those described for the experimental encephalitis of the other investigators. This had already been found to be true by Oliver[44] and, further, Flexner[16] called attention to the occurrence of spontaneous encephalitis in monkeys as described by Lucke.[36] Friedenwald[17] working with herpetic encephalitis observed a spontaneous encephalitis in a rabbit after some simple surgical procedure, having nothing whatever to do with the central nervous system, or with any encephalitic virus. Kling, Davide, and Liljenquist[31] obtained a virus from encephalitic patients which produced a chronic encephalitis in rabbits; these lesions are thought by Flexner[16] to be identical with some of the spontaneous lesions observed by him in non-experimentally infected animals.

In the meantime, Luger and Lauda,[37] experimenting with a filtrable virus of herpes simplex, found that it produced an encephalitis in rabbits. Doerr and Vochting[13] succeeded in confirming this and were able in addition to produce herpes again in rabbits with the filtrates of rabbit brain which had been infected with herpetic encephalitis. Doerr[13] indentifies this virus with the virus of encephalitis, obtained from epidemic encephalitic patients. He demonstrated that the herpes virus and the encephalitic virus (transmitted to rabbits) would cross immunize.

The evidence to date then consists of very conflicting experimental data: Loewe and Strauss,[38] with a very easily obtained, widely distributed virus; Levaditi and Harvier[35] with a similar virus but extremely difficult to obtain; the identification of the herpes and encephalitic virus by Doerr,[12] Flexner and Amoss[16] with complete failure; and finally the frequent finding of the pathological picture of encephalitis in stock animals by many investigators.

We are in no position to make a decision about these conflicting facts, but the evidence would seem to run to the effect that the etiological agent of epidemic encephalitis is not yet discovered, and that the described viruses are probably related to, or are identical with, the virus of herpes simplex.

Symptomatology and Course.—v. Economo's[14] original description of the disease, was, that it was a "sort of sleeping sickness," which for the most part ran a slow course; that headache and nausea, which were the initial symptoms, usually began acutely; and then appeared a state of somnolence, at times accompanied by an active delirium; from this somnolence the patient was easily aroused and could give a relatively good account of his surroundings, was able to execute commands correctly, and then, even while standing or walking, might fall again into a profound sleepy state. This delirious somnolence could, rapidly, or in the course of some weeks, lead to a fatal outcome; or it might persist for weeks or months, and then eventuate in improvement or complete recovery. The disease might or might not at this stage be accompanied by fever and it was quite possible, although unusual, to have its entire course afebrile. To these general symptoms are to be added, paralytic symptoms, especially pareses and paralyses of muscles supplied by the cranial nerves; and in particular the eye muscle group—ptosis, diplopia, and involvement of the various other eye muscles.

This original account of the disease, although it describes accurately a large group of cases, which have come to be regarded as typical, nevertheless has had to be much augmented and amended in order to include the multifarious manifestations of the disease. Of outstanding importance is the fact that somnolence and lethargy may not only not be necessary symptoms, but that the opposite symptom of sleeplessness may be the most pronounced.

The onset of the disease in children as well as in adults is, as Bardach[3] has said, almost always uncharacteristic; and only as the symptoms increase and develop day by day does the disease become really recognizable. The initial general symptoms may come on gradually over a period of days, or they may appear quite suddenly. At the onset, the symptoms are apt to be essentially signs of general systemic infection. The children complain of headache, fatigability, loss of appetite, nausea and vomiting, restlessness, irritability, and vague pain in the abdomen or extremities. Although all of these signs may be present, it is quite possible that all initial symptoms may be completely absent. The illness is often mistaken for a gastrointestinal upset or an attack of influenza—especially if, as is the rule, the disease is accompanied by fever. The temperature may be high (105–106 degrees) or may be only slightly elevated above normal (99–100 degrees). Usually it is only moderately elevated (101–102 degrees) and it may be intermittent, remittent, or continuous.

After these original signs of general infection have appeared, symptoms referable to the central nervous system become manifest. The most frequent of these signs are diplopia (double vision), drowsiness and sleepiness, and ptosis. The ptosis may vary from a slight paresis of the eye lids, with a feeling of lid heaviness, all the way to complete ptosis. It may be unilateral or bilateral, and in the latter case may affect the two sides of the face unequally. The somnolence and lethargy may vary from slight drowsiness, to very profound sleep or even to coma. The readiness with which the patients can be aroused from their somnolence and lethargy and the apparent wide-awakedness and clearness when once they are awakened, is a very striking quality of the lethargy. The sleep, however, is overpowering, and the patients are apt to promptly fall asleep again, while being examined, or even when they are standing or walking. At the beginning, or while the first neurological signs are developing, the disease may be accompanied by a very active delirium—a delirium which, as a rule, has fear and depression, Hohman,[26] as its dominant mood. The child may be actively hallucinated, often goes through the motions of its play, acts as if it were in the schoolroom or imagines itself in some terrifying situation.

In addition to the eye signs already described above, very frequently palsies of the other eye muscles appear, uni-, or bilateral, internal or external strabismus; lateral or vertical nystagmus; or very remarkable nystagmoid-like movements in which there is a violent jerking of the whole eye ball backward and forward (antero-posteriorly) —movements which are in all probability myoclonic, Kudelski and Sicard.[53] There may also be marked difficulty in convergence, or disturbances of other associated eye movements—Happ and Mason[22] described one child who could not rotate the eyes above the horizontal plane and one of my cases can not turn the eyes low enough to see his belt. Paralysis of accommodation, or failure of the pupils to react to light, either Argyll-Robertson, or the reverse, are not uncommon. Irregular pupils or unequal pupils are frequently present. Dimness of vision is often seen and in rare cases may be caused by an optic neuritis, Symonds.[57] Disturbances of the other cranial nerves are very frequent, especially the facial (seventh) with unilateral or, more rarely, bilateral facial weakness; the hypoglossal (twelfth) with deviation of the tongue to the right or left; and less frequently the trigeminal (fifth), is involved so that one obtains marked masseter tenderness (a very characteristic sign when it is present), trismus, and also numbness or tingling of the face; the glossopharyngeal and vagus (ninth and tenth) with marked respiratory irregularity or hypernea (without acidosis), Harrop and Loeb,[25] tachycardia or bradycardia, dysphagia and dysarthria. Hiccough of medullary origin may be very prolonged, persisting for weeks and months.

The facies often have a blank or mask-like expression, and there may be general hypertonicity of all the musculature, which at times reaches a very high grade of rigidity. This rigidity may be akin to those of extrapyramidal origin (Parkinson-like), or may be like that accompanying meningitis; in other cases it is of a more functional variety, like that seen in the catatonic states. The meningitic form is often accompanied by neck stiffness and Kernig's sign and may lead one to suspect an actual meningitis; while the functional sort frequently shows a waxy flexibility and commands automatisms.

These symptoms are apt to present themselves in the most bizzare, kaleidoscopic, pleomorphic fashion and a sign, present at one examination, is gone when the child is examined a day or even an hour later. The attack may be of so abortive a nature that after a few days of illness, the child is allowed to return to school or to play, only to show a recrudescence of symptoms in a few days or weeks.

The fever, if present, is often extremely variable. It may be constant for days or months or disappear for varying intervals of time only to reappear again. The severity of symptoms or the protraction of the course seems to have no relation to the temperature variations. The neurologic signs may be equally variable, and practically every combination of the symptoms mentioned, in different time sequences has been reported.

A great number of attempts have been made to classify this varying symptomatology of the disease under types; for example Hoffstadt[27] recognized five clinical types: (I) A pure encephalitic form with (*a*) acute choreatic, (*b*) myoclonic lethargic, (*c*) choreo-athetotic form, (II) a Landry's ascending paralytic form, (III) a meningitis form, (IV) a myelitic form (rare), (V) an abortive form.

Tilney and Howe[59] describe eight clinical types: (I) Lethargic, (II) cataleptic, (III) paralysis agitans, (IV) polioencephalitic, (V) anterior poliomyelitic, (VI) poliomyelitic, (VII) epilepto-maniacal, (VIII) acute psychotic, and 11 anatomical ones:

(I) Cases with general nervous system involvement with scant or fleeting localizing signs, (II) meningitic, (III) cortical, (IV) pyramidal system, (V) thalamic, (VI) corpus striatum, (VII) brain stem, (VIII) cerebellar, (IX) spinal, (X) peripheral nerve, (XI) multiple diffuse lesion types.

These classifications betray their weakness from the fact that they reach completeness only by including every part of the nervous system, and, nearly every possible type of neurologic disorder. Furthermore, the great majority of cases present symptoms which must be included under several groupings and, therefore, it seems to us wiser to subscribe to the opinion of those observers, who recognize a wide distribution of nervous system involvement, and have described symptoms as such; holding the question of the localization of these symptoms to be very doubtful in a disease in which the nervous system is so extensively and multifocally involved.

The most common symptom of the general neuro-motor system irritation is abnormal muscular contractions which grade from single twitchings of individual muscle fibers through myoclonia to profound choreas, athetoses, (Goodhardt),[18] dystonia, (Goodhart & Kraus),[19] and convulsions. The muscular twitchings although they may be merely fibrillary and are to be seen in only isolated muscles, much as one finds in the progressive muscular atrophies, usually, involve entire muscles and are much more myoclonic in form. Isolated lightning like contractions in the abdominal musculature have been so striking a symptom that it has, in fact, been regarded as a diagnostic sign by Reilly.[50] The twitchings may be unilaterally restricted, or involve both sides of the body as for example in the case of a young boy, observed by us, who had practically every muscle of the body involved by fibrillary twitching, together with a marked dysphagia and dysarthria. It was only because of the occurrence of the case during the epidemic of encephalitis and because of his rapid complete recovery that the condition could be distinguished from an acute muscular atrophy. The contractions of the muscles, may be rhythmical or non-rhythmical, and may be moderately slow or lightning like. The rapid, repeated twitchings, uncontrollable and persisting in sleep, have been usually called myoclonia. The chorea-like movements are at times indistinguishable from those of true Syndenham's chorea, except that the movements are apt to be much more violent—in fact so violent as to practically throw the child out of bed, Bardach.[3] In some cases these choreiform movements involve only one-half of the body and at times only one of the extremities. The choreatic movements instead of having a violent or lightning-like character, may be slower and more rhythmical and then take on an athetoid appearance; or they may involve certain larger muscle groups causing simpler and less bizarre movements than athetosis and have a more purposive appearance. These movements which, however, are not voluntarily controllable and always repeat the same pattern are those which have been named dystonias. As example, one of our patients showed constant slow rhythmic raising of the shoulder, abduction of the arm, with flexion of the elbow and partial supination of the hand; another showed frequent, rhythmic, repeated movements of flexion at the knee; and still others have involvement of the diaphragmatic musculature. Convulsions are not common but are not rare at onset; and epilepsy with petit and grand mal may occur as a sequella.

Although in adults, paralyses other than those of the cranial nerves, are relatively rare, they are not so infrequently seen in children. Hemiplegia, diplegias, Patterson and Spence,[48] paraplegias, Happ and Mason,[22] and monoplegias have been observed. These paralyses may be accompanied by definite pyramidal signs (loss of abdominal reflexes, increase of deep reflexes, and positive Babinski sign) or these signs may be absent and the involvement may manifest itself only as a slight paresis or weakness. Apert[2] reports an interesting transitory paraplegia in a child of 12. Other cases show typical peripheral nerve involvement with monoplegic paresis, numbness and parasthesia, atrophy, and nerve tenderness. Crookshank[7] and many others have reported cases of acute ascending paralysis of the Landry type—that is, an ascending flaccid paralysis without sensory loss or sphincter disturbance. It should be here noted incidentally that sphincter disturbances are extremely rare in any stage of epidemic encephalitis, even during the course of the acute delirious phases. To this large list of motor disturbances tremor of many sorts must be added. This usually involves the hands and lips and is usually a coarse type, but it may be fine; and the tremor may even suggest an intention tremor, Grossman.[20] Parkinson-like syndromes, although they may be seen in the earlier part of the disease make their appearance in the great number of cases long after the acute attack, and will, therefore, be discussed below under sequellæ. Although I have not seen a typical pseudo-bulbar syndrome except in adults, cases have been described with explosive laughter and weeping, Sicard and Paraf.[52] The marked asthenia as well as the ataxia, v. Economo,[14] that causes staggering and uncertainty of movement, has been regarded as being a cerebellar component of the disease process. A type resembling myasthenia gravis has been described by Hall.[21] Sensory disturbances are rare as far as reduction of sensation is concerned, although occasionally one sees paresthesia, numbness, and analgesias of a slight and transitory variety. On the other hand excruciating lightning-like pains especially in the lower extremities are not uncommon and these have been described under the heading of an "acute descending radicular type" and are probably due to posterior root involvement. The chief symptoms, according to Pardee,[16] are (1) "sharp lancinating root pain, (2) paresthesias, (3) muscular spasms, (4) hyperasthesia, (5) delirium, (6) fever." Cases have also been described with a syringomyelia type of sensory dissociation, Kennedy et al.[29] Vasomotor changes are not common except for excessive sweating which is a prominent symptom and at times is extremely severe. This sweating usually involves only the forehead and lips but may involve the whole body; in rare cases a hemihyperhidrosis is seen. Curious localized chills with pilomotor erection (goose flesh) has been described, Kennedy et al.[29] Increased salivation, although usually an accompaniment of the Parkinson syndrome may occur early in the acute stages and be very marked.

Various observers have reported a variety of exanthemata and erythema at the onset of the disease: Petechial rashes, miliarial rashes, herpes, and desquamation by Crookshank;[7] impetiginous eruption, and scarlatiniform rashes, Happ and Mason.[22] These rashes may at times cause serious confusion in diagnosis.

The mental side of the clinical picture is not only unusual but very often one of the most disturbing features of the disease. The most common of these manifestations is a marked sleep disturbance. This consists essentially in a reversal of the sleep curve, Blackfan and Happ[23] so that instead of sleeping at night, the children stay awake until three, four, and five o'clock in the morning, and then sleep soundly until very late the next morning. Hoffstadt[27] thinks that in addition to the reversal of the sleep curve, that there is actually a lengthening of the 24 hours' sleep rhythm as well. The behavior of the children during the nocturnal wakefulness is very extraordinary. Children who have played quietly all day and have been tractable in school or about the house, as soon as they go to bed, seem suddenly to be released from all inhibition and instead of being drowsy and quiet, begin a cycle of very unusual behavior; they whistle or sing or talk to themselves, and toss constantly about the bed; they pat and rearrange the pillows, take the bed clothes off the bed, and then replace them again; or get up and march around the room; or run up and down the stairs; grit and grind the teeth; cry out with piercing yells; have attacks of respiratory disturbance and rapid puffing and blowing, or irregular breathing. These children make no complaints of pain or discomfort. They simply can not go to sleep, and no matter what amount of exercise they are given during the day, or whether they are awakened early in the morning or are forced to stay in bed or are allowed to be up, this reversal of the sleep with this odd behavior period continues to exist. Hypnotics must be used in large doses to induce earlier sleep and as soon as they are abandoned the difficulty recurs. This inverted disturbed sleep may persist for weeks or months and then suddenly or gradually disappear with no apparent change in the general course of the disease.

During the acute stage, intractable insomnia may be encountered and seems to be a very ominous sign (it accompanied only fatal cases in our series, and others report the same experience).

During the early stage a characteristic symptom is a great overtalkativeness, Hohman.[26] Words pour out in veritable torrents and often, this overtalkativeness is not accompanied by any oddity of thinking, expression, or activity. In some cases there may be great overactivity as well and the child presents then a typical hypomanic picture. In some cases the overtalkativeness and overactivity may persist for years—as long as four years in one of my cases. Depression states, Bardach,[3] also accompany the acute stages and one should be very cautious about leaving the children alone, because of the danger of self-inflicted injury. Acute anxiety or fear states may accompany the depression and the children often feel sinful and beg and cry for forgiveness, or talk about death, or heaven and hell. Still others show states almost indistinguishable from acute catatonic stupors, with waxy flexibility, command automatism, mutism, and other schizophrenic oddities of behavior.

Delirium is also a very frequent concomitant of the acute period. The cases show all gradations of confusion from a slight uncertainty of orientation to profound clouding and stupor, and this delirium is very apt to be colored by fear and hallucinatory experiences of various sorts.

One must recognize that the disease, in general, shows step-like progression in the increase of symptoms. After an apparent stationary period one suddenly gets a new crop of symptoms, only to be succeeded a little later by a recession of these or earlier ones and then again another crop of new ones.

Sequelæ.—Although it is possible that all the disorders which are to be described as late manifestations of the disease may occur either full-blown or as fragments in the acute stages of the disease, yet the fact that they so frequently appear after abortive infections (so mild as to be regarded only as attacks of mild influenza or even after unrecognized infections), and, because they may occur after long intervals (one to five years) of apparent health, makes this separation justifiable at least for clinical purposes.

Although a classification of the symptomatology of these late residuals is difficult, nevertheless, certain of them form well-defined clinical manifestations, which can be considered under the following headings: (1) Behavior and mental disorders, (2) sleep disorders, (3) Parkinson-like syndrome, (4) tics, choreas, athetoses, (5) paralytic and convulsive residuals, (6) endocrine syndromes and vasomotor disorders.

1. The post-encephalitic behavior disturbances have been reported by various observers, Leahy and Sands,[33] Hohman,[26] et al., but do not seem to have been as well recognized as definitely post-encephalitic, as they should have been. Children are still regarded as bad rather than as sick because many physicians do not know that this type of incorrigibility is a frequent result of encephalitis. Children who were formerly tractable become unaccountably stubborn, untruthful, disrespectful, unruly, and incorrigible. They destroy everything they touch, refuse to stay at home or go to school, stay out late at night, and are utterly refractory to training or discipline. They may be careless of excreta and may actually smear the walls and floors with urine and feces. They tease and torment their playmates and animals and the degree of their misbehavior may actually amount to criminal activity, such as, stealing, threats of murder, sexual misdemeanors with exposure, peeping, and overt sexual precocity; some of these children have been so difficult to control that even mental hospitals find themselves almost unable to cope with the problem. Discipline, no matter how severe, is completely unavailing. A curious exception to this sequence of events is reported by Grossman[20] who found one child who changed from an incorrigible to a mild, peaceful, well-mannered boy. A less serious form is seen in a number of children who have shown change in their work habits so that they are later found to be lazy, shiftless, distractible, and unreliable, although previously they had been industrious, stable, and dependable. It is obvious that where such serious cerebral involvement has occurred, mental defect is often found. Retardation of from three to four years or even more pronounced defect, is frequently discovered after the attack is over. A number of children have become chronic "complainers" and have aches and pains all over the body, without any demonstrable organic lesions.

2. The sleep disturbances are similar to those already described under the acute stages. This reversal of the sleep curve may persist for months or even years. Hofstadt[27] reports an interesting pair of children who showed marked slowing and Parkinson's syndrome by day, and wakefulness and overactivity at night. Another group of children fall asleep during the day and the teachers report that in the middle of a class they find the child sound asleep.

3. *Parkinson-like Syndrome.*—Although the mask-like ironed out facies is typical in the acute stages of the disease, and although a moderate degree of general body rigidity may be present at this early date, the syndrome as a whole is preëminently a late sequela. As long as five or six years after the child has apparently recovered from the illness, or gradually after an infection so mild as to have completely escaped parental notice, the parents in the course of time observe that the child is slower in its movements; that its body is bent forward with the shoulders hunched over; that it salivates excessively; does not swing its arms in walking; that the arms are flexed at the elbow, and the hands are held in a peculiar position and may show a coarse tremor suggesting pill-rolling.) This peculiar hand position is a partial flexion at the carpometacarpal joints and extension at the metacarpophalangeal joints. (That there is also a tendency to run forward or backward and walking is slow with bent knees, and the gait is shuffling and uncertain. The mental reactions of the child are sluggish and labored and the speech is slow and monotonous. There is marked sweating of the face, particularly over the forehead. Gradually these symptoms increase in severity. This is the typical picture of the Parkinson syndrome. The neurological examination of the child shows practically nothing except an increase in, and a cog wheel-like, resistance to passive movements. There is no paralysis of the muscles and no alteration in the reflexes. The rigidity and fixity of position may be so great that the patient is actually bedridden, or can walk only with the greatest difficulty.

"Extrapyramidal" symptoms are also described and include fragments of the Parkinson syndrome alone or in conjunction with other symptoms. The most typical of the extrapyramidal symptoms are forced movements and positions, and positions of election. The forced movements include rhythmic alternate flexions of the leg at the knee; and forced movements of the eyes, lips, or jaws. The eye movements show forced upward or lateral conjugate deviations with or without forced movements of the head, Hohman.[26] The lips may show constant tasting movements and the jaws at times are seen to be constantly in rhythmic contraction; muscular dystonias, involving practically every large muscle group (e.g., bilateral and unilateral involvement of the muscles of the shoulder girdle, unilateral involvement of the arm, shoulder and face)—this is a slowly repeated rhythmical contraction usually resembling purposive movements.

Further, the arms may be carried in flexion as the position of election. This attitude can be relaxed when attention is drawn to it, but the patient spontaneously prefers this new position. Other patients show overflexion of the legs in walking, and exaggerated swinging of the arms.

One of our patients, a child with a Parkinson syndrome, can run but can not walk and as soon as he attempts to stand, he falls, by having his legs crumple under him. There is no paralysis or weakness but an apparent loss of the ability to stand. Other children show inability to initiate or stop movements when once initiated. A number of patients complain that their feet turn in on them. Various combinations of these symptoms are seen, e.g., dystonia of one arm and shoulder with Parkinson rigidity on the other side, and each period of time seems to be producing new combinations.

4. *Tics, Choreas, and Athetoses.*—These forced movements are closely akin to a certain group of symptoms, namely the tics and obsessive-like activities, which were formerly regarded as purely functional or psychogenic. We have now come to recognize them as having an organic basis of some sort, although the localization of the lesion remains very uncertain or if not completely unknown. It has been suggested that they are behavior fragments released by the loss of inhibitory control of the midbrain; but this has no substantial basis as yet. Between the tics and the forced movements it is difficult to make a clean cut distinction. We have a great variety of respiratory disorders which partake of the character of both. The children not only are forced to breathe more rapidly and with a change in the depth of respiration (either shallower or deeper) but they may also accompany the altered respiration with puffing and blowing and facial contortions. One boy described by Sicard and Paraf,[52] showed attacks in which he held his breath, threw back his head, and finally lost consciousness. Another showed marked breathing difficulty, along with hiccoughing, stretching, sobbing and uncontrollable laughter suggesting the emotional incontinence of a Wilson's disease or a pseudo-bulbar palsy. The hiccoughs may prove a very disturbing difficulty after several months duration, as may also rhythmical continuous coughing attacks. Habitual vomiting has been described.

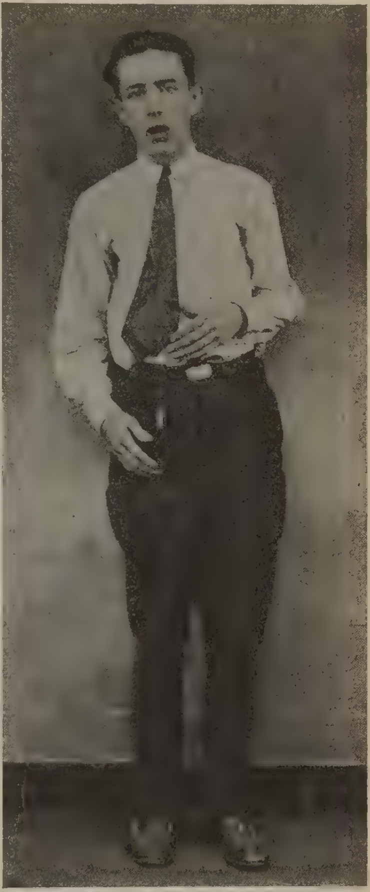

FIG. 336.—Position of left arm in flexion. "Position of election." Postencephalitic Parkinson syndrome.

As against these more organic looking symptoms we have tics and obsessive activity, Hohman.[26] Various children have been found to show intractable thumb sucking, spitting, stammering, nose picking, lip picking, touching the shoe and putting the hand in the mouth, rubbing the cheek and ear after wetting the fingers, shaking the hand, smoothing the hair, clucking movements of the tongue, "crossing" themselves in rhythms of 3, 9, or 27, and many more complicated bits of behavior.

Chorea initiated during the acute attack may persist for many months or years. It may be a hemi- or bilateral form or may involve only one member of the body. These choreiform movements may be like an acute Sydenham's chorea or may be more severe so that the movements are violent enough to throw the child out of bed.

The choreiform movements gradually shade over into movements of an athetoid character which usually involve the arms and at times the face.

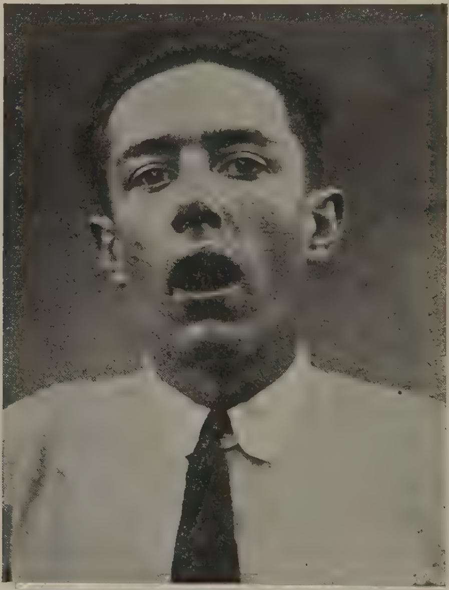

Fig. 337.—Parkinson facies. This patient has had a post-encephalitic Parkinson syndrome for 5 years. He is now 18.

Myoclonic movements of the face, extremities, diaphragm, and abdominal muscles may persist for months or years from the beginning of an attack or they may make their first appearance long after the acute stages are over.

5. *Paralytic Residuals and Convulsive Attacks.*—Although the ophthalmoplegias and facial palsies are apt to be transitory and shifting, yet one may find as long-standing residual, weakness of one side of the face, unilateral or bilateral ptosis of mild degree, internal or external strabismus, fixed or irregular pupils, and deviation of the tongue to one side or the other. There may be persistent dysphagia and dysarthria, and furthermore, although more rarely, hemiplegias,

diplegias, or paraplegias. These may have occurred at onset or later, and may or may not show signs of improvement. They are accompanied by the usual neurological signs of cerebral disease—Babinski's sign, rigidity with contracture, and paresis or paralysis. Disturbances of sensation in the form of paresthesia and tingling may exist along with the hemiplegia.

Long after the initial illness, epilepsy may develop with petit or grand mal attacks. These convulsive seizures may appear in very bizarre settings. I saw one child with very marked behavior difficulties and with violent temper outbursts, who, in addition to very painful stammering, showed a tremendous erotic drive. As soon as her erotic drive was thwarted in the slightest she would go into a rage, and then followed a series of 30 or 40 petit mal attacks between which she would try to kill or seriously injure the bystanders. The finalé to the performance would be a grand mal convulsion after which good behavior might persist for a short time. Epilepsy in our experience has been a rare sequela of epidemic encephalitis in contrast to nonsuppurative encephalitis in which it is so common.

6. *Endocrine and Vasomotor Disorders.*—Endocrine disorders have manifested themselves as a dystrophia adiposo-genitalis, Stiefler,[55] a diabetes insipidus, a hypertrichosis, or sexual precocity. Some of these children have grown enormously fat, with a failure of the genitals to show further development. Diabetes insipidus has been very troublesome especially when behavior difficulties have also accompanied it, because it is utterly impossible to control the ingestion of very large quantities of water. One case described by Kennedy, R. L. J,[30] developed a very severe hypertrichosis. Several of my patients showed a very early development of the sexual organs and one girl began to menstruate at nine. She had at that time well developed mammæ and pubic hair.

The vasomotor disturbances have been seen in excessive general or localized sweating, tachycardias, bradycardias, and unusual blushing and blanching.

Pathological Anatomy.—The pathological anatomy of the central nervous system has been sufficiently studied to present a fairly clear description, although this study has shed relatively little light on the question of the individual symptom and its anatomical representation in the nervous system. A few debatable conclusions have been reached but they represent no certainty or even uniformity of opinion.

The pathology of the acute cases was studied first by v. Economo[14] and his description was so nearly complete that very little has been added since, except in confirmation. He describes the meninges as only slightly involved, and this involvement no more marked at the base than over the convexity. There may be a mild hyperemia of the membranes, and a mild round cell infiltration especially about the vessels of the pia. At times, however, the evidence of meningeal irritation may be quite massive so that one may speak of a local meningitis. The pia and arachnoid maybe slightly opaque or milky according to Da Fano and Ingelby,[10] and meningeal hemorrhages are certainly not always present although they may be quite extensive, Buzzard and Greenfield.[5]

v. Economo[14] found the grey matter, above all, affected the cortex, the basal ganglia, the central grey, and the midbrain colliculi, the pons nuclei, the cranial nerve nuclei, and the grey matter of the spinal cord. Although all parts of the nervous system are affected the predominance of midbrain and basal ganglia lesions is quite striking.

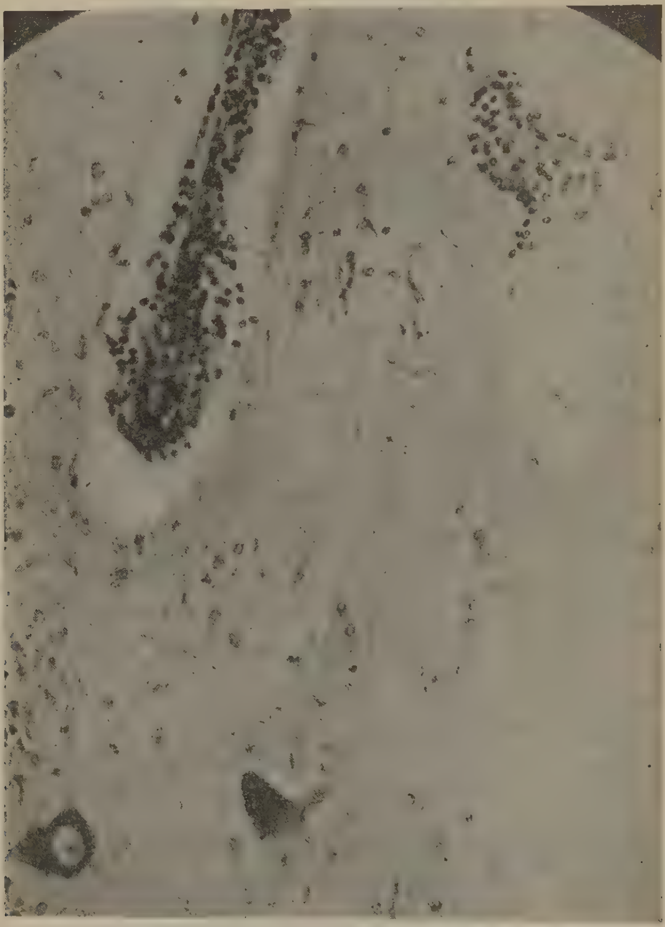

FIG. 338.—Blood vessel from the anterior horn region of the spinal cord showing round-cell infiltration (acute epidemic encephalitis).

On section of the brain one finds evidence of congestion, with minute hemorrhages, and bloody mottling of the chief areas affected. At times there may be a very mild hydrocephalus, Hall.[21]

The microscopic findings show three striking changes: (1) Small-cell infiltration in and about the adventitia of the blood vessel, especially the veins, (2) focal areas of cellular infiltration in the parenchyma of the grey matter, (3) marked "neuronophagia" about the ganglion cells.

The vessel wall infiltration is primarily in the Virchow-Robin's spaces and is made up in part of lymphocytes, plasma-cells, polyblasts, and occasionally a polymorphonuclear leucocyte. Fat-granule cells are rarely seen, except in cases in which hemorrhages or softenings are present. The cellular infiltrate may be so massive as to completely obscure the architechtonic configuration of the region. The glia is apt to show marked proliferation and in large areas of infiltration there may be so great a richness of cellular elements, as to suggest abscess formation, especially if a large number of polymorphonuclears are present. The ganglion cells show varying degrees of alteration

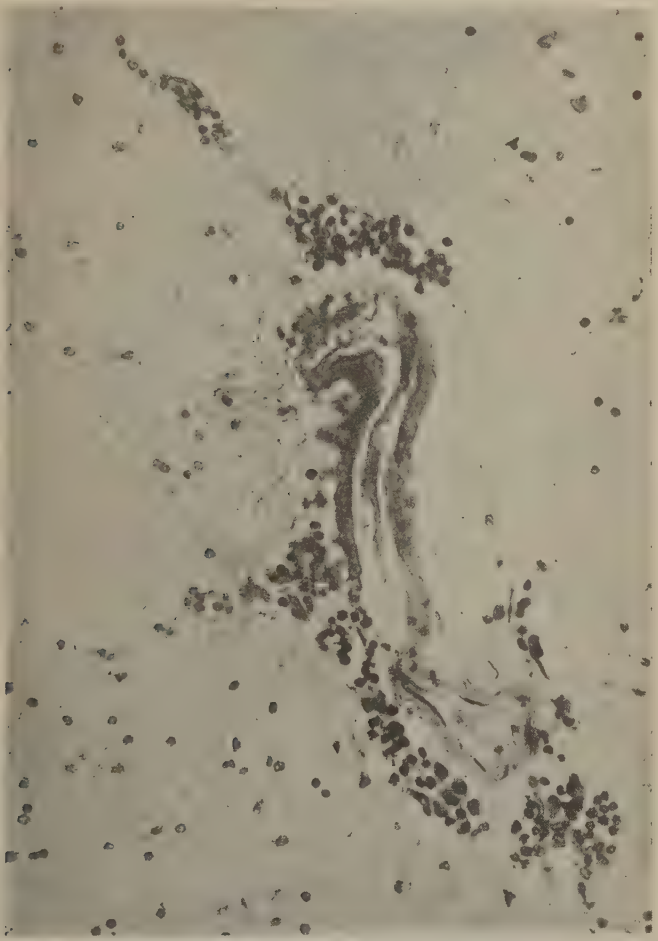

Fig. 339.—Blood vessel from the hypothalamic region showing adventitial cell infiltration, hyalinization of the vessel wall, and colloidal material in the lumen of the vessel (acute epidemic encephalitis).

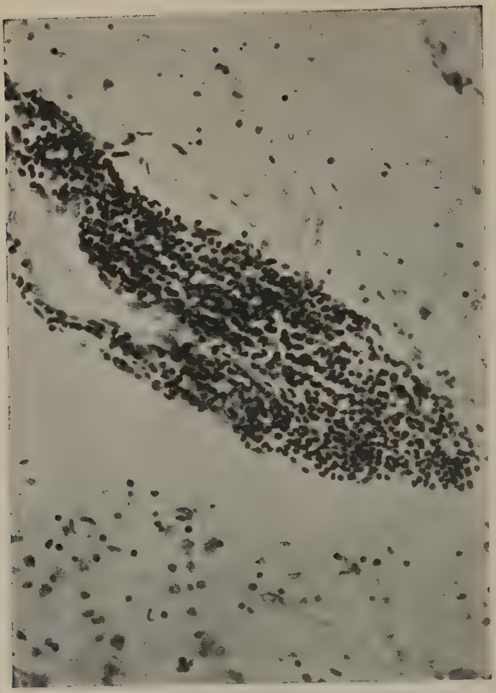

Fig. 340.—Massive meningeal infiltration from the spinal cord region (chronic epidemic encephalitis).

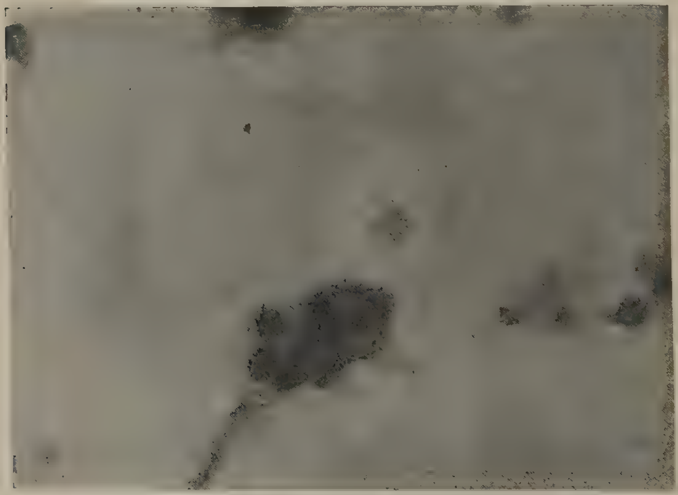

Fig. 341.—Pyramidal cell from cerebral cortex showing "neuronophagia" (chronic epidemic encephalitis).

from mere dissolution of the Nissl substance, to lysis of the nuclear membrane, and dissolution of the cell boundaries. Glial cells surround these diseased cells and appear to be phagocytizing them. This is known as neuronophagia and is held by practically all investigators to be one of the cardinal features of the pathological process. Marinesco[41] has also described thromboses in the small venules.

Besides these degenerative manifestations v. Economo[14] found reparative processes as well. In the area emptied of parenchyma by the infiltrate there was evidence of the new growth of connective tissue cells from the vessel walls.

In cases which have shown tendency to healing, the meninges are slightly thickened, but no longer hyperemic, the blood vessels still show perivascular infiltrate but the character of the cells has changed—they are mainly round cells with only an occasional plasma cell. The white matter shows only rare cellular infiltration, but a marked increase in glia elements, rich in processes and tending to pile up in certain areas as foci of glia cells (glia knötchen). The evidence of permanent ganglion cell damage is clear. Certain of the cells are atrophic or sclerosed in addition to the ones which are in the process of being destroyed. The myelin sheaths are often swollen and in places much fragmented.

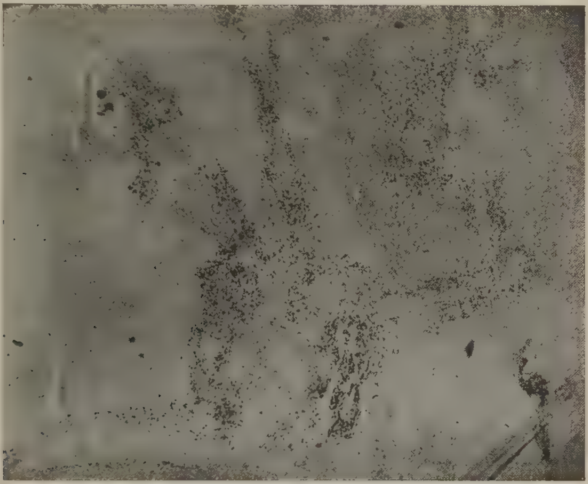

FIG. 342.—Pia showing round-cell infiltration. From the cerebral cortex in a chronic case (chronic epidemic encephalitis).

The study of chronic cases has been carried on mainly in those who have died during the course of Parkinson's syndrome. It was hoped that this group would yield important information regarding the localization of the anatomical lesion corresponding to this disorder of motor function but, unfortunately, it was soon discovered that the process was altogether too extensive to lead to any definite conclusion on that score. The writer recently has investigated, pathologically, a series of 12 of these cases[26] and has found that the only constant lesion is a degeneration, of more or less profound degree, in the pigmented cells of the substantia nigra. One case in particular yielded practically no lesion except a massive degeneration of the substantia nigra. Although this has been practically a constant finding by many investigators, it is impossible to reconcile it with the opinion of another group of workers, who from a different material, (non-encephalitic) place the lesion for the extrapyramidal syndrome of the Parkinson type in the globus pallidus and putamen. Further study will be needed to settle the controversy. It is quite possible that both are right—that the extrapyramidal motor pathway is made up of several links and that a break in one of several places may produce the same clinical

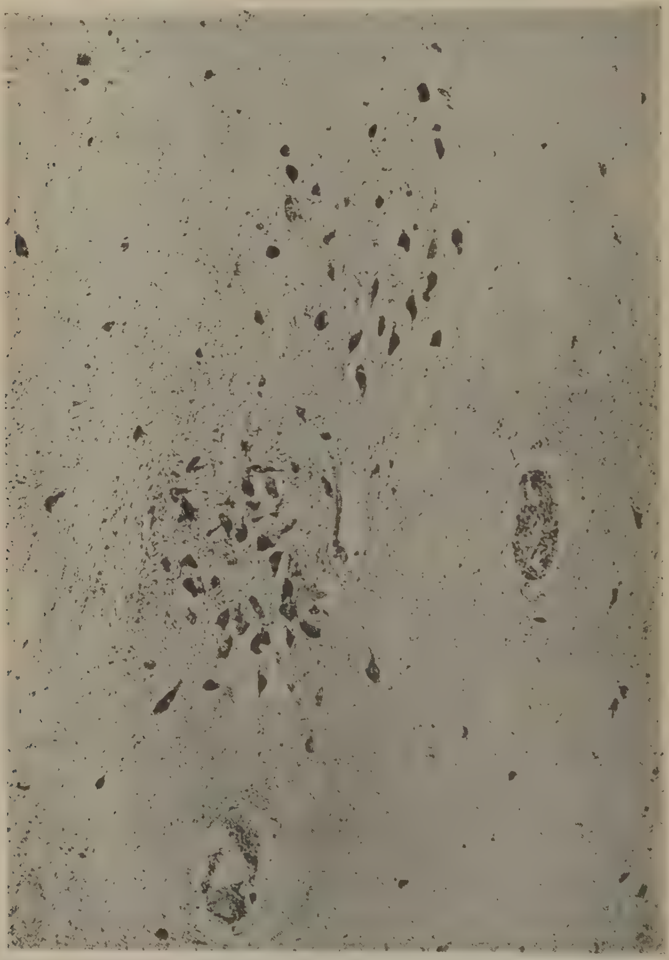

Fig. 343.—Substantia nigra from an acute case of epidemic encephalitis, showing round cell infiltration and in addition the normal configuration of the pigmented cells.

condition. Other outstanding facts resulting from our investigation of these chronic cases, are that indeed all parts of the nervous system show involvement; the process seems to be subacute even years after onset—the perivascular and interstitial infiltrate persists and contains occasional polymorphonuclear leucocytes—active meningeal irritation is often present; and the ganglion cells show evidence of active degeneration, as well as sclerotic changes. The absence of hemorrhages was very noticeable in all our cases. Furthermore, there was evidence of extensive fiber fragmentation and degeneration.

Fig. 344.—Substantia nigra from a post-encephalitic Parkinson's syndrome, showing practically complete disappearance of the pigmented cells, with only pigment clumps and pigmented glia cells remaining.

The understanding of the fleeting and transitory nature of the neurologic involvements needs explanation. Three have been suggested: (1) That considerable edema accompanies the process and that the symptoms disappear as the edema recedes, (2) that small hemorrhages may be absorbed promptly, or (3) that the virus may exert a temporary paralyzing effect without calling out sufficient cellular reaction to actually destroy the parenchyma.

The sleep disturbance and the lethargy have called forth much discussion and many hypotheses, *e.g.*, disturbance of a sleep center in the midbrain, or hypophysis, or basal ganglion, or thalamus, and it has also been suggested that increased intracranial pressure is responsible for the lethargy and somnolence. To date no real evidence, however, has been produced by the various cases and we must hope for the solution of this problem from some other source.

A final word about the minute bodies described by Da Fano and Ingelby.[10] These investigators found minute granules in the protoplasm of certain nerve cells which showed degenerative changes. These have also been found in herpetic-virus encephalitis by Da Fano[9] and by Levaditi,[35] et al. Da Fano[9] suggests tentatively that they represent the virus itself or that the virus may adhere to these minute bodies.

Differential Diagnosis.—The differentiation of this disease from other forms of central nervous system disease or from acute infections having cerebral manifestations may be extremely difficult. Neal[42] and Happ and Mason[22] feel that it is a diagnosis to be made by exclusion and this is certainly true if the case occurs, in the absence of an epidemic and without the symptoms of lethargy, somnolence, and cranial nerve palsies. It so closely follows the course of other diseases, especially of the nervous system, that often only post-mortem examination can reveal the true nature of the process. The problem may be very puzzling when the diagnosis must be made between this disease and (1) tuberculous meningitis, (2) cerebral tumor, (3) abscess, (4) non-suppurative encephalitis, or (5) epidemic poliomyelitis. More rarely one must differentiate between epidemic encephalitis and (6) brain syphilis, (7) typhoid fever with hebetude, (8) lead or other metallic encephalopathies, (9) epidemic meningitis, (10) hysteria.

1. *Tuberculous Meningitis.*—The onset in this disease is insidious, the temperature gradually rises toward the end, and death follows within three weeks. There is usually evidence of other tuberculous foci, and the spinal fluid shows a gradually increasing number of cells with tubercle bacilli in the films which form (if one is sufficiently diligent in the search). Of course, meningeal symptoms are prominent.

2. In the differentiation from *cerebral tumor* the condition presents difficulties which are of greater importance. In these cases the question of operative intervention arises. In general, it is my opinion, that when any real doubt exists, exploration or at least air injection by the Dandy method is desirable, because a delay in operation may be fatal. If fever is absent, and there is evidence of increased intracranial pres-

sure, with headache and vomiting, there is sufficient indication for surgical intervention, but one must remember that a similar group of symptoms may on rare occasions occur in encephalitis.

3. Probably most of the mistakes in diagnosis have been made by regarding *brain abscess* as epidemic encephalitis. The history of a severe injury, or an old suppurative otitis media, or mastoiditis, or fulminating sinus disease, together with high intermittent fever, and markedly increased leucocytes suggest the diagnosis of brain abscess. Relatively high cell count in the spinal fluid is also suggestive of abscess.

4. *Non-suppurative encephalitis* may occasionally puzzle one although the issue is largely academic. The sequelæ are equally disastrous in either case and therapeutically the differentiation is of no avail. Cranial nerve palsies are less common in non-suppurative encephalitis, hemiplegias the rule, and the occurrence after infectious disease usually makes the diagnosis relatively simple.

5. *Poliomyelitis* has a different seasonal incidence (a disease of summer and early fall). The paralyses which are more circumscribed, are spinal rather than cerebral in type, the pupils almost invariably react to light, and cerebral manifestations are rare. The reaction of degeneration is present in the affected muscles.

6. *Brain syphilis* usually offers no difficulty as soon as a lumbar puncture is done. The Wassermann is universally negative in encephalitis.

7. *Typhoid fever* with its general symptoms and positive blood culture or positive Widal reaction should confuse one only temporarily.

8. *Lead and metallic encephalopathies* may cause more difficulty but these are very rare conditions in children. The peripheral nature of the palsies, the abdominal colic and lead line, together with the changes in the red cells (anisocytosis, poikilocytosis, and stippling) could leave one in little doubt. The spinal fluid in lead encephalopathy gives a heavy globulin reaction with the Pandy test and the cell count is nearly normal.

9. *Epidemic meningitis* presents a much more rapidly fulminating course, more prominent meningeal signs, and the finding of a very large cellular increase in the spinal fluid, mainly polymorphonuclear, with diplococci in the leucocytes.

10. The differentiation from *hysteria* or an acute psychotic development has often caused difficulty in diagnosis. Children, who present no fever and no focal signs, are often thought of as exasperating and bad, and depression or overtalkativeness may be the only signs of the disease for weeks. Any alteration of the sleep curve, or sudden change in disposition or behavior, should lead one to be wary about excluding the diagnosis of epidemic encephalitis. Slight variations in ease of movement or the carrying of the arm in position of flexion, or a mask-like facies, may be the early signs of encephalitic residuals when the original attack has escaped notice.

Laboratory Findings.—The laboratory examinations are able to give only a limited aid to the diagnosis of epidemic encephalitis.

Blood.—The leucocytes vary from normal to 15,000 or 20,000, according to Neal[42] and there may occasionally be a leucopenia, Happ and Mason.[22] By and large the count is found to be normal or slightly increased. There is no alteration in the red blood cell count nor in the differential count. Blood cultures have proven uniformly sterile.

Urine.—Occasionally one sees a slight increase in albumen and a few casts but no more than one would expect to find as a concomitant of an acute infectious disease. The rare finding of sugar in the urine has suggested the explanation to v. Economo[14] that the disease is due to a medullary involvement.

Spinal Fluid.—Neal[42] in a study of 100 spinal fluids found them clear in practically every case. Occasionally a web formed, or the fluid was blood tinged suggesting a hemorrhagic form of the disease. The cells often were not increased over normal, but the usual finding was 10 to 15 cells. They ran as high as 1,500 (one case). The cells were predominantly mononuclear although polymorphonuclears were occasionally the main type. The sugar was not increased. The gold-sol curve (colloidal gold chloride test) was frequently altered but in no characteristic fashion. The pressure was usually increased. The Wassermann was uniformly negative.

Bardach[3] and Findlay and Shiskin[15] agree in these findings but found the sugar content increased and the latter found the cells never exceeded 20 and that the gold-sol curve was always altered. They all found globulin increased. Happ and Mason[22] found a fairly characteristic behavior of the number of cells in the spinal fluid. The cell count is usually normal at first or slightly increased, rises rapidly to a peak within a few days, and then drops to normal again. With these findings of Happ and Mason[22] my experience is in accord. I have seen cases with cells as high as 250 fall to normal in one week. Since lumbar puncture is possibly a favorable therapeutic procedure, one is justified in examining the spinal fluid frequently during the acute stages.

One can summarize the spinal fluid findings by saying that the fluid is usually clear, under some increased pressure, with a moderate increase in cells, an increase in globulin, and often an alteration in the gold-sol curve. It should, however, be born in mind that the fluid may be completely normal.

Treatment.—Hall[21] concludes his recent book on epidemic encephalitis with the following statement: "The evidence as to the real value of the methods of treatment advocated is difficult to estimate in a disease, the natural progress of which is so extremely irregular. The verdict on the whole, is that, at present, any reliable therapeusis, either for the disease or its many after results, does not exist." With this conclusion, we are in complete accord except as regards palliative treatment for the post-encephalitic Parkinson syndromes. Not only do we have no reliable or even promising therapy for the disease itself, but since we know nothing about its mode of contagion, we are powerless to suggest measures for the control of the spread of the disease. Isolation is to no point, because we know of no contact infection.

One can only devote attention to general nursing care. The food should consist, during the febrile period, of nourishing liquid diet, and gradually be extended as the patient improves. Gavage may have to be resorted to if the patient is too lethargic or stuporous to eat voluntarily. Constipation is the rule in the disease and should be treated by enemata or mild cathartics. Careful attention should be given the skin because with the increased sweating it is apt to be in poor condition, and bed sores develop readily. Sleep should be induced with paraldehyde or morphia if the patient has any tendency to insomnia, because protracted insomnia is a very unfavorable symptom.

The only rational therapy so far proposed is the use of convalescent serum. Although some cases seem to do well with it, the usual experience has been that the majority of cases show no benefit, and there is no evidence that the serum is responsible for the improvement that does rarely occur.

The following list of the remedies that have been suggested will give the correct impression that none could have been very useful: Urotropin by mouth, and intravenously; iodine in various forms—externally, intramuscularly and intravenously; arsenic in various preparations; mercury in a great many forms; trypaflavine; sodium salicylate; adrenalin; organic silver salts; use of fixed sterile abscesses to stimulate leucocytosis; autogenous intraspinous serum; antimeningococcal serum; immune streptococcal serum; lumbar puncture; etc.

The treatment of the residuals is almost as unsatisfactory. Children with behavior disorders have been quite intractable in my hands except in the cases where the parents were making the problem more difficult by spoiling the children further. Removal of these particular ones from their home environment has been helpful.

Veronal in 5-gr. doses and paralydehyde in 2-dr. doses may temporarily solve the sleep problem for those children with reversed sleep curve but this is useful only on occasions. It is wisest to readjust the sleeping time of the nurse or person caring for the child because otherwise they will obtain no sleep either night or day.

The treatment of the post-encephalitic Parkinson syndrome by hyoscin hydrobromide, has, in my hands, been very successful. Most of the failures to get results with hyoscin have been due to the fact that too small doses have been used. Most of my experience[26] has been with adults, in whom I have used doses as great as $\frac{1}{30}$ gr., and have given this dose four times a day (by mouth). Starting with $\frac{1}{150}$ gr. four times a day, I increase the dose by $\frac{1}{150}$ gr. a dose, at weekly intervals, until an increased amount fails to give any added relaxation of the rigidity or quieting of the tremor. I then drop to the last effective dose. I have no notion that the drug is anything more than a palliative remedy, but it has turned bedridden patients back to a useful life of work in many cases. Patients do not develop any tolerance to the drug and the same dosage can be used for months and years. An initial difficulty in accommodation and a sense of sleepiness, and occasionally a little nausea, are symptoms which soon pass, and I have had no patients who could not tolerate the drug. None have shown any really untoward effects. My experience with children although limited has been most satisfactory. Usually 1/100 gr. four times a day is sufficient to relax the rigidity, and to cause definite increase in mental alertness. I can recommend a most thorough trial of the drug. It has, however, proven completely useless in the other residuals.

(Hyoscin should be used with great caution in infants and young children. In children under three or four years of age, 1/1000 gr. should be the maximum initial dose and may be repeated two or three times daily, if required for further relaxation.—EDITOR)

Prognosis.—The prognosis during the acute stages as to actual life is extremely difficult to state. Practically every mode of onset has been reported by some investigators to be the most malignant and then later to be less ominous. In general the severe deliria, the cases that can not sleep, the severe myoclonic types, and meningitic forms, are apt to show the highest mortality. This, however, varies greatly from locality to locality, and from epidemic to epidemic. Mortalities from 7.4 per cent. to 50 per cent. in the same epidemic have been reported from different countries. It is clear that prognostications must be extremely guarded. This applies not only to the immediate outcome but also as regards the ultimate recovery without residual. As noted above, extrapyramidal syndrome may appear four to five years after the initial infection. Here again investigators differ. Zweigenthal[62] found only a minority of cases return to normal and Stadelman[54] found 89 per cent. completely recovered. The longer one observes cases, the more frequently one sees sequellæ. The course of the late manifestations is very variable, especially in children. The Parkinson syndrome does not seem to show any tendency to recovery at all, unless the rigidity be present during the acute stages. The behavior difficulties do show improvement in at least 50 per cent. of our cases. The sleep disturbances may exist for months and years but usually improve or disappear. The myoclonic phenomenon generally improve, but the athetosis, choreas, and dystonias on the other hand, do not show any tendency to disappearance. The tics and forced movements may give way, but are usually replaced by a more serious type of motility disorder. The mental states, except when actual defect occurs, have shown uniform improvement and recovery although it may require many months or years.

The course of the post-encephalitic Parkinson syndrome is usually a slowly progressive one—after the symptoms have received their initial full development. Gradually the patients lose weight, their rigidity increases, and when they become bed-ridden bed sores develop and intercurrent infections cause death. This course may, however, extend over several years, and if the patient is treated by hyoscin the condition appears to be held stationary in most of the cases.

On the whole, the disease must be regarded as one of extreme gravity.

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CHAPTER CXCV

ANIMAL PARASITES

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Definition.—An organism that lives either permanently or temporarily on or within the body of another living thing and draws nutrition from the latter is called a parasite. The organism from which it obtains sustenance is denominated the host. Evidently either the parasite or the host may be a plant or an animal, so that four groups of relationship may be established. The phytoparasites or plant parasites include especially the group of bacteria, with a few molds, yeasts, and other unicellular plants of etiologic importance. These will not be discussed within the present article, which is to be devoted to a consideration of the animal parasites of man, particularly those verminous parasites which attack human beings early in life, and thus are of especial importance in the study of children's diseases.

Parasitic organisms display all gradations from free-living forms to the most intensive parasitism. Temporary parasites, such as mosquitoes, bedbugs, and leeches, remain with one host only long enough to snatch a meal and then move on. Such organisms have in the main the structure, appearance, and habit of free-living animals, and in the simplest case differ little from carnivorous types. Indeed within the group of leeches are included species of carnivorous habits side by side with those of parasitic habits. In the extreme instance the individual species practices both habits at different times, in that it devours small aquatic animals but, when a larger animal is encountered, contents itself with sucking a meal.

Biological Relations.—Temporary parasites attack persons of all ages with equal readiness, although the child asleep in a crib or baby carriage is probably more likely than its adult guardian to be bitten by flies and mosquitoes. Individual differences in sensitiveness and perhaps also in attractiveness to the biting insects become evident in any considerable group of people. So far as has been established, however, no one of these biting insects preys particularly on children to the exclusion of older persons.

Other insect parasites, such as lice and fleas, are more definitely adapted to the parasitic habit than mosquitoes and flies. They remain longer on one host and only occasionally seek to effect a change. While possessing some power of migration, they show greater similarity to permanent parasites and greater modifications from the typical free-living insects than do the mosquitoes and flies. Owing perhaps to a certain indifference to hygienic conditions displayed by children, the latter are more likely than adults to be infested by parasites of this type. No special discussion of insect parasites is included in the present article. However, within recent years there has accumulated abundant evidence of their importance as transmitters of certain diseases caused by microscopic organisms which are introduced through the agency of biting and sucking insects.

Ectoparasites.—The species just described are all parasitic upon the exterior of the host, and are denominated, ectoparasites or epizoa. The ectoparasites of man belong to the group technically designated as Arthropoda and include in addition to the insects, of which several different types were enumerated above, the mites and ticks, which are in some cases transmitting agents for protozoal or bacterial diseases.

Endoparasites.—The parasites inhabiting internal organs—in which they secure much better shelter from mechanical injuries and, at the same time, larger opportunity for extracting nutrition from the materials within the cavity inhabited, or through the thin membranes lining that cavity—are by virtue of their location designated the entozoa or endoparasites. With the exception of a few very rare forms, these do not belong to the same subdivisions of the animal tree as do the ectoparasitic forms. The human entozoa include the single-celled animalcules or Protozoa, and the various types ordinarily designated as worms, *viz.*, the flukes or Trematoda, the tapeworms or Cestoda, and the round or thread worms, the Nematoda. Most of these are highly specialized as parasitic organisms, and indeed so firmly adjusted to the parasitic habit that they cannot exist as free-living organisms.

The endoparasites of man are not closely related genetically, as they are included in several distinct branches of the animal kingdom. While they are similar in a biologic sense, in structure they are often more closely related to free-living species than to other parasitic types. The groups of Protozoa and Nematoda both contain free-living and parasitic forms and sometimes even closely related genera or species manifest this difference in habit. Among the Trematoda and Cestoda, however, all of the forms are parasitic and no authentic cases of free-living forms are recorded. Statements to the contrary, as those of Linnaeus that tapeworms up to 300 ft. in length have been found occasionally in springs or brooks, rest, in so far as they are not figments of the imagination, on the discovery of individual parasites accidentally discharged from the host and thus found swimming about freely in the water.

The alimentary canal is the primary seat of endoparasites and the liver and the lungs are nearly equally involved. It is, however, venturesome to attempt the identification of any parasite on the basis of the organ in which it is discovered. The majority of parasites confine themselves to a distinct location, but some species occur in a wide variety of different organs. Even in these, one organ can usually be designated as the normal location of the species, whereas the other parts of the body affected are reached only by erratic individuals of the species.

Erratic Parasites.—Those parasites which, though they may be in the normal host, are present in an unusual location are designated as erratic. In this class belong the occasional cases of Cysticercus in the brain and of liver fluke in a subcutaneous cyst. One may also rightly include in this class forms which are normally parasites of some other species but have by chance been introduced into the human host and accommodate themselves to conditions there. Instances of this relation in children are recorded. Thus the abundant and cosmopolitan tapeworm of both dog and cat (*Dipylidium caninum*) has been found several times in man. Almost all of the cases concern children, and there is little doubt that the infection was due to intimate intercourse between the children and pet animals. Evidently this species does not become a human parasite under ordinary circumstances merely because it is not brought in contact with the human host at a time in its life history when transfer is possible. Improved methods of hygiene and greater care for environmental conditions will possibly ultimately result in eliminating these cases in children. In the case of *Ascaris maritima*, a parasite described by Leuckart from a single specimen vomited by a child in Greenland, Blanchard noted it was much like *A. transfuga* of the brown bear and conjectured that it was ingested with the viscera of some animal used as food, such as the seal.

LIFE HISTORY OF PARASITES

The life history of the parasite determines the manner in which it can gain access to the human species, the probability of its accomplishing this end successfully, and the ratio of infection. Thus the lungworm of the pig is an exceedingly common parasite throughout all of Central Europe, and yet it is almost unknown as a human parasite. Properly introduced, it can hold its own and becomes, for the time being, a normal parasite of man; but the extreme rarity of such cases indicates that conditions in the life history block access to the human host and reduce human infection to exceptional instances.

The development of parasitic forms is regularly complex, even though a few species show direct development of a simple type. In the majority of cases, complications have arisen that bear a very precise relation to some phase in the development or habits of the host. Thus the larva of the human blood fluke has a free swimming stage with a boring apparatus to penetrate the skin. In consequence, bathers in the open water are readily infected, and in Egypt, where bathing in the open is general, the human host shows a very high percentage of infestation. And there is no other method of infecting the host.

The development of parasites is likely to be characterized by a complexity of different generations, associated in many cases with different hosts. This alternation of generations and of hosts renders the history difficult to trace; yet on its solution depends the possibility of combating successfully the disease, since the parasite must be prevented from gaining access to the human host, rather than fought after it has established itself.

Complexities.—One finds, in fact, all degrees of complexity. In some of the nematodes of the human alimentary canal the development seems to be direct. The eggs gaining the exterior with the dejecta of the host are carried about by chance. Development proceeds within the shell until, through the medium of impure water or uncooked foods, the egg, enclosing now a well-developed embryo, is transported automatically into the human alimentary canal. Here the embryo hatches out, undergoes transformation, and achieves the adult condition by simple growth. In some cases the juvenile forms of the parasite exist in one portion of the canal and, when sexually mature, pass on to reproduce in another portion.

Thus, for instance, while the pinworm grows to maturity in the ileum, the ripe female migrates to the cecum and from there makes periodic excursions to the rectum, where oviposition is carried out. In other species, as in *Ascaris lumbricoides*, the larvæ hatched in the intestine wander out into the tissues, and only after a period of growth and change do they return to the alimentary canal to pass their adult life. A variation on this method is seen in the development of the hookworm, which enters the tissues through the epidermis and reaches the alimentary canal for the first time at the conclusion of its migrations and of its growth period. In other forms there is hatched from the egg a free-living larva that passes a portion of its existence in the external world and returns in a more advanced stage of development to complete its life history within the host.

A new type of complexity is added by the introduction of an intermediate host, in which the larval parasite passes the first period of its existence and from which it is transferred actively or passively to the primary host.

The process of simple development becomes more complex and stereotyped until the parasite never comes in contact with the external world but is transferred passively from the intermediate to the final host. This is well illustrated by the development of various filariæ and of trichina. The process may become even more involved, for certain flukes make use not merely of a single intermediate host but also of a second and third, so that three host species and transfers are involved in the complete life cycle. The supposed simplicity of development may be due, in fact, to imperfect knowledge of the situation; and some species which were long regarded as having a direct development have now been shown to pass through more complicated stages in completing their life history. The life history and habits of the parasite are precisely attuned to those of the host or hosts involved in the completion of the life cycle.

TRANSMISSION OF PARASITIC DISEASES

A parasitic disease is acquired in the simplest case by the ingestion by one host of spores or eggs produced in another. In some cases such spores are carried in drinking water; in others they are adherent to uncooked food articles. In still other instances they are borne in a dried or inactive condition, as dust in the air, and may be taken in through the respiratory organs or introduced accidentally into the digestive system. In more complex cases some other agency is concerned with the transport of these intermediate stages. The eggs of parasites may be carried by flies and introduced into environments to which they would otherwise not find access.

Flies play an important part hitherto underestimated in the transport of intestinal parasites. Though long known as regards Entozoa, this has only recently been demonstrated in striking fashion for Protozoa. Cysts or eggs die very slowly in the fly; therefore flies are important agencies in carrying disease-producing organisms from feces to human food. As the fly feces dry out very rapidly, the only considerable danger is encountered when the flies defecate on moist or liquid foods. If infected flies are drowned in soup, milk, water or other liquid food, human beings may be infected by the accidental ingestion of such food. The instrument, *i.e.*, the insect concerned in such occurrences, is purely incidental, and not in any necessary fashion related to the life history of the disease-producing organism.

Blood=sucking insects, however, play often an essential part in the transmission of certain diseases, in that the insect itself becomes infected and serves as a host for the disease producing organism until that stage is reached in which the organism may again be transmitted to the human host. This method of transport provides at once the greatest protection for the disease-producing organism and the greatest assurance of its proper introduction into the human host. These conditions obtain in some of the most widespread and serious of human diseases.

Liability of Children to Parasitic Infection—In all of these cases it will be evident that children are distinctly more liable to infection than adults. They acquire disease by chance more readily by virtue of indifference to personal hygiene and the character of their surroundings as well as carelessness in the selection and handling of food. They are also more likely to suffer because they do not guard themselves so well against the bites of insects and are not able to prevent recurrence of the attack. Besides they are less completely protected by clothing and are hence more exposed to attack. Age susceptibility is discussed later in this article.

Manner of Infecting the Human Host

The introduction of a parasite into the human host is, from the standpoint of preventive medicine, the most significant feature in the life history of the parasite; and the elucidation of the life cycle gives the proper clue as to the time and manner in which this introduction takes place, as well as suggests the means by which the infection of the human host may be prevented. The discovery that the bladder-worm encysted in beef was the early stage of the human tapeworm demonstrated the source of infection, namely, the eating of such meat as had not been sufficiently cooked to kill the bladder-worms. The discovery of larval trichinæ encysted in the muscles of the pig pointed toward the consumption of imperfectly cooked pork as the origin of trichinosis. Most of the worm parasites which are common in the human host are introduced thus directly with food.

Opportunity for Infection.—Chance plays a large part in the introduction of human parasites. Grubs, hair worms, maggots, and even tapeworms have been collected from wells and from running water. Some forms occur frequently in fruit, others in old or carelessly handled meat, and some, such as mites, in cheese and on fruit. Accordingly any or all of these parasites may at times be carried directly into the human alimentary canal. If able to withstand the conditions even for a brief period, such animals may become apparent residents of the alimentary canal. They are, however, only incidentally parasitic.

Contamination of Food.—Other less frequent or less well-known species with larval stages in insects like the cockroach or meal-worm, are probably introduced by chance through the contamination of food articles by such infected insects. In children, the disregard of personal cleanliness or lack of fastidiousness is responsible for the introduction of species that are either unknown or very rare in adults, who are naturally more careful than children. The practice of biting the finger nails, or of sucking fingers or toes, introduces material with which the child has unconsciously come in contact; this is the method by which is introduced among others the larva of *Dipylidium caninum*, of which the adult lives in the dog and cat, and the larva in the fleas which infest those domestic animals. The contamination of the hands with eggs or larvæ from dirt is a frequent means of infection for children and field laborers. A study of 800 white and 500 negro school children, aged from 6 to 18 years, indicated that unconscious coprophagy is common. This varies to an appreciable extent in the same town, being less among people living at homes provided with sewers than among those who use privies. Part of this coprophagy is due to filth carried to the food by flies, and part is due to contamination of food by cooks; part thereof is also undoubtedly dependent on the personal daily habits (of play, for instance) of the children, and the figures indicate that there is a greater difference in this respect between the white girls and boys than among the negro children.

Contamination of Water.—The water supply is doubtless responsible in many cases for the introduction of eggs and embryos. The primitive habit of securing drinking water from surface sources affords adequate opportunity for contamination by parasites. It has been proposed to estimate the purity of drinking waters in a district by determining the degree of parasitic infestation of the population. But in Cayenne, M. Leger found that 70 per cent. of the children aged between 1 and 12 years, carried intestinal parasites, even though typhoid is rare and the city water of conspicuous purity. Hence the importance of the drinking water alone may be easily over-emphasized.

Uncooked Food.—Solid and uncooked foods are usually dangerous, especially is this true where human excrement is utilized as fertilizer or where an indifferently guarded water supply is depended on. At one time, direct infection was considered the major means by which the human host was reached, and numerous species were said to be transferred directly to man. Additional information concerning the life history of parasites shows that many of these cases are not so simple. There still remain, however, a number of instances in which, so far as is now known, this must be the method by which man is infected.

Social Organization.—The abundance of parasites in man has varied with changes in social organization. Among savage tribes individuals were too widely separated to permit parasitic diseases to become serious; for whenever conditions became threatening, the infected locality was abandoned for the new habitations free from infective agents. Moreover, constant movement kept infection at its lowest level. Such conditions can be seen among the nomad tribes today. When the human race abandoned its nomad life and began to concentrate in small communities, the incidence of human parasitic infection increased greatly. Parasitic epidemics became frequent and demanded a heavy toll from these primitive communities. Failure to appreciate the importance of a proper water supply or of adequate precautions in the disposal of waste led to the general infection of the population. Rain and wind distributed widely those eggs which were protected from adverse conditions by an impermeable shell and contaminated the surface water over large areas. Of course, this contamination was more frequent and more severe near the larger settlements and in the more densely populated areas, so that as population increased and the communities grew more crowded, parasitic diseases also multiplied in number and importance. The case became slightly more complicated when the human host was not infected directly but through the medium of an intermediate host.

Effect of Social Progress.—When attention was directed to the purification of water supplies, and in consequence an adequate amount of well-selected and thoroughly protected water became available for domestic purposes, these diseases declined in importance. As municipal and personal cleanliness increased, the percentage of parasitic infection greatly decreased. The employment further of footgear and general clothing reduced the likelihood of infection or the abundance of entozoa, until many parasitic diseases were banished from the more fastidious part of human society and occurred primarily, if not exclusively, among field laborers or others whose occupations brought them most directly in contact with sources of infection.

The decrease of intimate association with domestic animals, especially dogs and cats, has reduced the percentage of parasitic infection among highly civilized nations or groups.

The Effect of Cooking.—Cooking of food is possibly the most influential factor in limiting the number of parasites and in shutting off entirely certain avenues of approach to the human system. Civilized man uses cooked foods more largely than savage or semicivilized people use them. Were all animal food to be eaten only when thoroughly cooked, the common tapeworms and the much feared trichinæ would cease to be of clinical importance. In direct correspondence with this view, one finds the beef tapeworm unusually common where beef is eaten rare, and the pork tapeworm where pork is not subjected to thorough cooking. Among those nations by which raw fish is esteemed a delicacy, the fish tapeworm is common. Where this habit does not exist, the fish tapeworm is practically unknown. Regional prejudices or established customs should always be taken into account in the efforts to determine the source of parasitic infection, and the method by which it is to be avoided. Of course, success depends on the willingness to abandon prejudice or to change habits of life which are often very deeply rooted in the individual character. That these factors are of real significance in dealing with children's diseases cannot be doubted when one considers that often even infants are fed scraped uncooked beef, raw fish, or smoked but uncooked ham.

Immunity.—Some studies have been made to determine whether the human host can acquire any immunity to zooparasitic diseases but the results are far from final. Racial (acquired?) immunity appears to be present in some cases. The negro is apparently less affected by the hookworm than the white man. Variation in age susceptibility has been definitely proved in schistosomiasis and probably ascariasis, children being much more affected than adults. But the variation does not hold for all parasites and its cause is far from clear even in these two diseases.

The dog hookworm can be found in certain regions in almost every pup less than a year old but is rare in older dogs. Inasmuch as the opportunities for acquiring the infection increase so directly with age that older dogs ought to be well infected, the reverse condition can be easily explained only on the basis of an acquired immunity.

The same reasoning applies in the case of children except that habits change to some extent with passing years. Careful studies have shown that in Europe among boys and girls in the first two five-year periods the order of incidence of parasitic infection is Ascaris, Trichuris, Oxyuris; but in the 10–15 year period it is Ascaris, Oxyuris, Trichuris. Other less clearly demonstrated changes with advancing years may be seen in the tables of frequency of parasitic infection.

PRENATAL INFECTION

Infancy offers no barrier to parasitic infection, according to the observations of Rousseau* among the natives in the forest region of Cameroon. In children under one year Ascaris and Trichuris were common though hookworms were not found, whereas for all ages the average infection was Ascaris 40 per cent., Trichuris 33 per cent., and hookworm 62 per cent.

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* Rousseau, Bull. soc. path. exot., 12: 244; May 14, 1919.

When parasites are reported as present in infants, one may consider most naturally that the parasite was acquired by some chance very early in life, even in the first few weeks or days after birth. But not all recorded instances can be explained in this way. In some cases the condition is certainly due to prenatal or congenital infection.

Among the Trematoda numerous cases are collated by Cort, who quotes also the work of Fujinami and Nakamura. These authors examined the feces of 22 newborn infants in an area in which *Schistosoma japonicum* was endemic and found the eggs of this species in three. Only one other trematode, the Japanese lung fluke, is known to have migrating larvæ, and this is the only other species in this group which might be a source of prenatal infection. However, no cases are known. Prenatal infection by cestode larvæ is infrequent though cases are recorded for echinococcus and less positively for cysticercus invasions of very young infants. It is among the nematodes that prenatal infection is most likely to occur.

Larval Migration.—Prenatal infestation may readily be brought about during the extensive migrations in the life cycle of Strongyloides, Ascaris and related forms. In fact the transfer of larvæ by the blood stream and their migrations through tissues will probably carry them often into the fetus when the mother suffers from a heavy infection. Neveu-Lemaire is of the opinion that congenital infestation with Ascaris, Ancylostoma, Strongyloides, and indeed with all forms of bursate nematodes, is much more frequent than is generally supposed, especially in warm countries. Yokogawa has demonstrated intrauterine infection with Ascaris in dogs only two days old.

Howard has reported an undoubted case of prenatal infection with hookworm in a negro infant. The eggs of the hookworm were found in the infant's feces 14 days after birth, a period too brief for the development of the adult if, as is very unlikely, infestation had taken place immediately after birth. The mother was seriously infected by the hookworm and suffered from ground itch. Howard cites also several cases of hookworm disease in Ceylon among infants one year old or younger. Cases of probable prenatal infection are also recorded in accounts of trichinosis.

FREQUNECY OF ANIMAL PARASITES

Widely divergent views are expressed regarding the frequency of intestinal parasites. While it may be true that their frequency has diminished greatly in recent years, owing to the introduction of measures for personal hygiene and municipal sanitation, yet as Moore states, this is more apparent than real and concerns the urban child rather than the rural child. Statistics, collated for this article from all available sources, show clearly that verminous parasites are very abundant not only among primitive peoples and in tropical regions but also in highly civilized nations. In the United States, for instance, among institutional children the incidence of intestinal parasites varies from 15 to 90 per cent., and almost everywhere the percentage is higher than is generally believed. In the same table are included findings from Central America, West Indies, and South America.

In the Tropics.—Such parasites are most frequent in tropical territory. In 1908 Garrison, as the result of his own studies, stated that the population of the Philippine Islands presented a higher percentage of infection with intestinal worms than had ever been definitely reported from any other people. In 1909 Garrison and Llamas reported intestinal parasites in practically all of the children examined. In 1920, Haughwout and Horrilleno substantiated this report, adding important details to the picture. Neither trematode nor cestode infection was found and, what is even more remarkable, no clearly pathogenic protozoa were demonstrated. Among 100 children ranging in age from 7 months to 13 years, 87 per cent. of 53 girls and 98 per cent. of 47 boys were parasitized. Of children under 1 year of age, two-thirds were infected; of those between one and two years, 74 per cent. were infected, while the group aged from 2 to 13 years showed 100 per cent. infection. The youngest child infected was only seven months old, and it harbored *Ascaris lumbricoides* and Spirocheta (Table 4).

Similar reports come from other tropical regions, but it is to be noted that they concern particularly the native population and that Europeans in the same regions are not as heavily infected. Thus Clapier* reported from the examination of stools in Liberia and Guinea that 154 native children of from 5 to 15 years harbored hookworm (75 per cent.), Ascaris (37 per cent.), Trichuris (35 per cent.), and Strongyloides (7 per cent.); whereas of 11 European children in the same district only three were infected and those with Trichuris alone.

In Europe.—A wealth of evidence obtained in many widely separated regions indicates that the degree to which European people, and especially children, are infected with helminths has increased greatly since the war and with serious results. Both the number of persons infected and the number of parasites in individual hosts have grown remarkably. Perhaps the most striking illustration of this is given by Härle, Sütterlin and Zeiss,† who as members of the German Red Cross in Russia made a careful study of 1500 children in asylums and at clinics in Moscow. They compare their results with those obtained by Grechaninoff before the war. The figures which I have combined in Table 4 indicate clearly the changed conditions without further analysis. Similar increases in worm infection of children are reported by others from other parts of Europe.

Relative Incidence.—The incidence of parasites varies widely in different persons in the same locality, where it bears a definite relation

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* Clapier, Bull. soc. path. exot., 10: 260; 1917

† Härle, A., Sütterlin, Th., and Zeiss, H., Helminthologische Untersuchungen an Moskauer Kindern. Zeitschr. f. Hyg. u. Infek.-Kr. (June, 1923), 100: 140.

TABLE I.—FREQUENCY OF

Data from North

Locality	Authority	Date	No. exam.	Type of host	Persons infected	
					No.	Per cent.
New York City	Schloss, O. M.	1910	280	C	85	30.3
New York City	McLean, Stafford	1920	308	C	7	2.27
Dist. of Columbia	Stiles and Garrison	1906	C 123 A 3334	M ..	26 349	21.13 10.43
Chicago Ill.	Murphy, W. W.	1906	102	C	7	6.86
Southern U. .S.	de Buys and Dwyer	1919	595	C	317	53.27
Montgomery, Ala.	Greil, G. J	1911	665	C	425	36.1
Texas	Judkins, O. H.	1912–14	15,000	M	....	....
Texas	Frey, J H.	1915	270	C	128	47.4
Guatemala	Un. Fruit Co. Rept.	1915	1971	M	....	....
Honduras (Tela)	Un. Fruit Co. Rept.	1914	774	M	....	....
Nicaragua	Molloy	1918	19,786	M	....	....
Costa Rica	Un. Fruit Co. Rept.	1914	6212	M	....	....
Canal Zone	Darling	1911	285	A	200	70.4
Panama	Un. Fruit Co. Rept.	1914	1971	M	....	....
Panama	Burres	1914–18	93,286	M	....	....
Cuba	Un. Fruit Co. Rept.	1914	36	M	....	....
Martinique	Noce, F.	1911	225	A	....	....
St. Lucia	Branch	1918	5004	M	....	....
St. Vincent	Gardner	1915–18	21,430	M	....	....
Trinidad	Payne	1918	40,482	M	....	....
Seychelles	Kendrick	1917–18	18,058	M	15,311	....
Porto Rico	Ashford, King and Gutierrez	1904	4482	M	4482	100
Colombia	Un. Fruit Co. Rept.	1915	428	M	....	....
Colombia	Brosius and Bishop	1920	600	A	....	....
British Guiana	Dershimer	1918	11,719	M	....	....
Brazil	Hackett	1918	10,490	M	....	....
Brazil	de Almeida, Jr.	1923	687	n	459	66.81
N. Brazil, Amazonas	da Matta	1910–21	1850	C	1620	87.56
Brazil (Capital do Amazona)	de Almeida, Jr.	1923	883	n	635	71.9
Brazil (Sao Paulo)	Ferreira (1)	1920	196	C	....	....
Brazil (Barra Funda)	de Almeida, Jr.	1923	1177	n	1078	91.6
Brazil, (Rio de Janeiro)	de Faria	1911	1238	C	662	53.4
Brazil, (Rio de Janeiro)	de Almeida, Jr.	1923	196	n	....	....
Argentine (Paraná)	Araujo	1924	4911	C	....	75*
Buenos Aires	Ferreira	1920	196	C		

Percentages are based on total number of persons examined.

(1) = All children under 12 years of age.

* Approximate percentage of children from 1 to 10 years of age infected.

INTESTINAL WORMS IN MAN
and South America

Trichuris trichiura		Oxyuris vermicularis		Hookworms		Ascaris lumbricoides		Strongyoides stercoralis		Hymenolepis nana		Taenia	
No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
31	11.07	23	8.21	....	....	6	2.14	....	....	20	7.14	5*a*	1.78
....	......	3	0.9	....	....	4	1.29	....	....	.....	....	......	....
16	13.01	2	1.63	1	0.81	1	0.81	....	....	6	4.88	......	....
267	8.00	45	1.34	36	1.07	17	0.53	8	0.29	12	0.35	2*a*	0.06
4	3.92	....	....	....	....	2	1.96	....	....	.....	....	1*a*	0.98
209	35.1	41	6.89	18	3.0	86	14.62	40	6.72	55	9.25	......	....
5	0.75	5	0.75	177	26.75	27	4.06	....	....	38	5.75	......	....
28	0.018	561	0.375	3844	25.6	42	0.028	4	0.0026	71	0.047	67*a*	0.045
6	2.2	16	5.9	155	57.4	....	....	....	....	88	32.1	1*a*	0.04
358	18.11	....	....	879	44.6	525	26.6	76	3.90	.....	....	3	0.15
73	0.94	....	....	80	1.03	17	0.021	21	0.027	.....	....	......	....
10,783	54.5	672	3.4	15,017	75.9	14,918	74.8	243	1.3	.....	....	145n	0.75
1048	16.87	41	0.064	1172	18.8	403	0.65	123	1.19	.....	....	......	....
133	46.6	4	1.4	98	34.09	8	2.81	5	1.76	.....	....	......	....
226	11.45	2	0.01	124	0.62	81	0.41	67	0.34	.....	....	......	....
18,343	20.2	126	0.013	13,656	84.4	36,407	39.1	15,187	16.2	.....	....	203n	0.022
8	22.22	....	....	3	0.83	....	....	7	19.4	.....	....	......	....
86	38.0	Several	....	83	36.8	110	44.0	....	....	1	0.04	Several	....
2002	40.0	....	....	3126	62.5	1681	33.5	1751	34.9	.....	....	......	....
15.729	73.4	....	....	955	85.4	19,501	91	2271	10.6	.....	....	1n	0.023
11,956	29.5	134	0.33	10,828	80.4	13,281	32.8	2705	6.68	.....	....	11n	0.002
17,028	94.3	3	0.001+	15,575	86.27	12,694	70.3	487	2.7	.....	....	......	....
326	7.27	3	0.007	4482	100	1408	31.41	36	0.08	.....	....	3*a* 1*o*	....
24	0.56	9	0.02	76	17.7	50	11.6	91	21.26	.....	....	1	....
204	34	1	0.16	390	65.0	253	40.3	61	10.6	.....	....	2*a*	0.30
2009	17.1	....	....	8727	74.5	3428	29.3	536	4.6	.....	....	......	....
....	......	....	....	6922	65.9	....	....	....	....	.....	....	......	....
159	34.7	33	0.72	89	1.89	181	39.44	....	....	36	7.86	......	....
896	48.43	340	12.90	1270	68.64	822	49.63	....	....	.....	....	......	....
522	82.3	192	30.2	604	95.2	331	52.2	151	23.9	.....	....	......	....
44	23.0	44	23.0	....	....	44	23.0	....	....	.....	....	......	....
765	64.99	18	0.15	127	1.70	516	43.84	90	0.76	108	0.92	20	0.16
446	36.02	11	0.09	120	0.98	432	34.08	58	0.47	.....	....	22*a*	0.18
156	80.0	156	80.0	....	....	156	80.0	....	....	.....	....	......	....
3975	80.9	... ...	....	4100	83.4	4498	91.5	....	....	.....	....	......	....
105	54	105	54	....	....	105	54.0	....	....	.....	....	......	....

Abbreviations used: A = Adults; *a* = *Taenia saginata;* C = children; M = mixed; n = no data given; *o* = *Taenia solium.*

TABLE 2.—FREQUENCY OF
Data from Africa,

Locality	Authority	Date	No. Exam.	Type of Host	Persons infected	
					No.	Per cent.
Queensland (Australia)	Waite	–1918	14,577	M	.....	....
Philippine Isds	Strong	1901	2179	M	.....	....
Philippine Isds	Mendoza	1910–16	1000	C	159	15.9
Philippine Isds	Tenney	1913	150	M	.....	....
Philippine Isds (Coll. Med. & Surgery)	Crowell and Hammack	1913	500	M	.....	Over 90.0
Philippine (Manila)	Garrison	1908	4106	M	3447	83.94
Philippine (Manila)Bilibid Prison	Garrison and Llamas	1909	385	M	.....	59.0
Philippine (Bilibid Prison)	Rissler and Gomez	1909	1087	M	760	70.0
Philippine, Bilibid Prison, Manila	Willets	1914	7843	M	5420	69.1
Philippine Gen. Hos., Manila	Willets	1914	1000	M	848	84.8
Philippine Civil Hospital Baquio	Chamberlain, Bloombergh and Kilbourne (1)	1910	183	M	183	100.0
Philippine (Taytay) typical town	Garrison, Leynes and Llamas	1909	1000	M	959	95.9
Philippine Isds. (Cavite Prov.)	Stitt, E. R.	1911	69	C	.....	....
Philippine Isds. (Las Pinas)	Rissler and Gomez (2)	1910	6018	M	5406	89.83
Philippine Isds. (Tuguegarao, Cagayan)	Rissler and Gomez (2)	1910	2594	M	1923	74.13
Philippine Isds. (Santa-Isabel, Illagan & Isabela)	Rissler and Gomez (2)	1910	802	M	692	11.40
Philippine Isds. (Baguio, Benquet)	Chamberlain, Bloombergh and Kilbourne	1911	119	A	110	92.5
Philippine Isds. (San Antonio & Mal., Ill., Isabela)	Willets	1911	4278	M	3656	85.46
Philippine Isds. Batanes Ids	Willets	1913	400	M	400	100
Philippine Isds. Cebu. Hosp	Garcia (2)	1917	1063	M	707	66.5
Formosa	Maxwell, J. L.	1908	1050	M	952	90 49
Korea	Kwun and Koboyashi	1917	326	C	323	99 07
Korea	Kojima and Ko (3)	1919	1000	M	1000	100 0
China	Day, E. and Olsen (5)	1908	500	M	305	61 0
China, Hongkong	Bell, J. (4)	1912	850	M	351	41.29
China, Peking	Faust	1918–19	....	n	.....	....
China, Shanghai	Day	1910	100	M	..	......
China, Shanghai	Faust	....	....	n	.....	....
China, Anking	Taylor (6)	1910	67	M	.....	....
China, Nanking	Faust	....	....	n	.....	....
China, Amoy	Faust	Average	....	n	.....	....
China, Canton	Faust	1919	....	n	.....	....
China, Chefoo	Faust	1919	....	n	.....	....
China, Shaoshing	Faust	1920	....	n	.....	....
China, Tsinan	Faust	1919	....	n	.....	....
Siam	Kerr, W. F. J. (7)	1916	250	A	.....	....
India	Dobson	1893	1249	n	.....	....
India	Fearnside	1900	878	n	.....	....
India	Calvert	1901	100	n	.....	....
Ivory Coast	Sorel, F.	1911	320	n	279	87.0
East Africa (Mombasa)	Shircore, J. O. (8)	1917	1500	A	778	51.8
Br. Cent. Africa	Daniels	1901	255	n	.....	....
West Africa	Wellman	1904	310	n	.....	....
Algeria	Soulie and Derrieu (9)	1916	316	C	155	49.05
Sahara (Barbary)	Foley, H. (10)	1911	214	M	.....	....

Percentages are based on total number of persons examined.

(1) Amoeba, 12 cases or 6.6 per cent.; Trichomonas, 1 case or 0.6 per cent.; *Distomum hepaticum*, 1 case or 0.6 per cent. Of the total number examined 100 were school children under 15 years of age.

(2) Protozoan findings included in total number of infected persons.

(3) Clonorchis 4.42 per cent.; Metagonimus 0.21 per cent.; Fasciolopsis 0.01 per cent.; Trichostrongylus 2.94 per cent.; Paragonimus 0.20 per cent.; Ascaris canis 0.08 per cent.; Unknown forms 16 per cent.

(4) Clonorchis 12.9 per cent.; Type of host, 197 Europeans of whom 47 were infected, 253 Indians of whom 79 were infected, 400 Chinese and Japanese of whom 224 were infected.

(5) Opisthorchis 2 cases or 0.4 per cent.; Fasciola 2 cases or 0.4 per cent.

(6) Schistosoma 11 cases or 16 per cent.

(7) Opisthorchis 17.0 per cent.; Ancylostoma 14.8 per cent.

INTESTINAL WORMS IN MAN

Australia, and Asia

Trichuris trichiura		Oxyuris vermicularis		Hookworms		Ascaris lumbricoides		Strongyloides stercoralis		Hymenolepis nana		Taenia	
No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	~~No.~~	Per cent.
183	1.25	75	0.51	2627	22.5	18	0.001	19	0.001	51	0.03	......	......
Very common		Several cases		54	2.48	Commonest		13	0.006	....	.....	Present	
42	4.2	4	4.0	4	4.0	152	15.2	...	....	....	.....	......	......
67	44.6	...	.....	50	33.0	48	32.0	...	....	....	.....	......	......
172	34.4	5	1.0	83	16.6	206	41.2	...	....	....	.....	1*a*	0.20
2426	59 0	32	0.80	2135	52.0	1052	26.0	132	3.0	5	0.10	30	0.70
300	87.6	2	0.60	46	13.45	182	53.22	...	....	0	0.0	1*a*	0.30
435	40.0	...	....	181	16.7	408	37.5	.....	....	....	.....	......	......
2553	47.1	...	.....	1203	22.2	2217	40.9	.....	....	....	.....	......	......
606	60.6	..	.....	187	18.7	465	46.5	.....	....	....	.....	......	......
53	29.0	4	2.2	53	29.0	39	26.3	1	0.6	....	.....	4*a* 5*o*	4.92
770	77.0	4	0.04	116	11.60	829	82.90	7	0.04	....	.....	......	......
51	75 3	. .	.....	.....	......	62	89.8	.....	....	....	.....	......	......
3241	53 40	298	4 95	671	11.14	4647	77.21	135	2.24	....	.....	4*a*	0.06
672	25.90	68	2.62	208	8.01	1907	73.55	...	....	19	0.73	13*n*	0.50
50	16.23	10	1 24	364	45.38	486	60.59	...	....	6	0.74	11*n*	1 37
72	60.0	...	.....	35	29.00	87	73.00	...	....	....	.....	15*n*	12.0
342	7.99	64	1.50	2326	54.37	2653	62.04	4	0.09	5	0.12	59*n*	1.38
187	46.7	...	.....	.....	25.5	.....	92.8	.....	....	....	.....	......	......
291	41.1	...	.....	221	31.3	187	27.8	.....	....	....	.....	......	......
516	49.05	...	.....	446	42.39	807	76.7	.....	....	....	.....	......	......
302	92.8	1	0.30	127	0.39	226	69.6	127	39.1	....	.....	30*n*	9.50
937	93.7	6	0.06	539	53.9	765	76.5	...	....	....	.....	72	0.72
120	24.0	2	0.4	27	5.4	273	54.6	1	0.2	....	.....	......	......
92	26.2	...	.....	47	13.3	164	46.6	...	....	....	.....	1	0.012
......	0	...	0.62	.....	3.8	.....	30.8	...	....	....	.....	......	3.47
21	21.0			15	15.0	54	54.0	.....	....	1	1.0	......	......
......	1.6	...	.....	.....	1.1	.....	11.6	...	....	....	.....	......	0.04
19	28.0	...	.....	24	36.0	47	70.0	...	....	....	.....	......	......
......	5.0	...	.....	.....	10.4	.....	34.9	...	....	....	.....	......	0.05
......	11.0	...	Common	.....	11.0	.....	78.0	...	Common	....	.....	......	Known
......	10.6	...	.....	.....	1.9	.....	29.2	...	....	....	.....	......	......
......	37.0	...	1.8	.....	17.4	.....	48.9	...	....	....	0.11	......	......
......	13.7	...	.....	.....	6.9	.....	33.9	...	....	....	.....	......	......
......	1.5	.....	0	.....	0.6	.....	40.0	...	....	....	.....	......	0.15
71	28.3	125	50.0	236	94.3	146	58.2	43	17.0	....	.....	146*a*	58.3
55	4.40	192	15.37	944	75.58	131	10.49	...	....	....	.....	18*a*	1.44
61	6.95	...	.....	578	65.83	282	32.12	..	....	....	.....	......	......
12	12.0	9	9.0	83	83.0	39	39.0	...	....	....	.....	......	......
22	6.8	...	.....	238	75	5	1.5	...	....	....	.....	7*n*	2.1
313	40.2	2	.....	347	44	270	34.7	2	....	2 nana —3 1 diminuta—	.....	168*n*	21.5
7	2.79	...	.....	25	9.96	15	5.98	3	1.20	....	.....	......	......
......	......	...	.....	13	4.13	158	50.97	2	0.65	....	.....	2*a*	0.65
77	24.3	11	3.4	.....	......	45	14.1	...	....	64	20.2	......	......
28	13		Rare	.....	......	178	83	....	....	9	4.2	6*a*	2.8

(8) Schistosoma 32 cases, 29 *S. mansoni*, 3 *S. haematobium.*

(9) Type of host, 309 European or native Jewish children, 7 native Moslem children.

(10) Schistosoma 12 cases or 8.0 per cent.

Abbreviations used:

A—Adults, *a*—*Taenia saginata* , C—Children, M—Mixed, n—No data given, T*o*—Taenia solium.

TABLE 3.—FREQUENCY OF INTESTINAL WORMS IN MAN

Data from Europe

Locality	Authority	Date	No. Exam.	Type of Host	Persons infected		Trichuris trichiura		Oxyuris vermicularis		Hookworms		Ascaris lumbricoides		Hymenolepis nana		Taenia		Diphyllobothrium latum	
					No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Eng. and Cornwall	Boycott	1904	98	n	....	.....	38	38.78	2	2.04	4	4.18	12	12.24						
Lisbon, Portugal	Paes	1918	503	C	272	54.	225	45.	11	2.	....	.....	91	18.	33	6.5				
Italy	Cima	1893–96	110	n	50	45.45	41	37.27	7	6.36	....	.....	31	28.18	7	6.35	1*a*	0.91		
Germany, Bonn	Gottberg	1919	200	C	126	62.5	....	.....	Very High		....	.....	Very High							
Dresden	Müller	1852–62	1939	n	....	.....	50	2.57	43	2.21	....	.....	180	9.28						
Erlangen	Müller	1862–73	1755	n	....	.....	195	11.11	213	12.13	....	.....	227	12.93						
Griefswald	Heisig	1893	230	n	114	49.56	104	45.21	Common		....	.....	34	14.78	....		1*a* 1*o*	0.43		
Kiel	Gribbohm	1872–77	972	n	482	49.80	313	32.20	226	32.20	....	.....	178	18.31						
Kiel	Heller	1872–75	611	n	291	47.62	187	30.60	142	23.25	....	.....	108	17.67						
Kiel	Sievers	1887	2629	n	....	.....	521	19.81	326	12.40	....	.....	436	16.58	....	.....	8*a*	0.30		
Munich	Banik	1886	315	n	126	40.31	26	8.25	95	30.16	....	.....	23	7.30	....		4*a* 1*o*	1.58		
Munich	Friedrich	1887	107	n	19	17.76	10	9.34	3	2.80	....	.....	7	6.54						
Russia	Gubareff	1896	486	n	325	66.87	212	43.62	4	0.82	....	.....	110	22.63	....		8*a* 4*o*	2.46	33	6.79
Kostroma	Grusdeff	1892	260	n	119	45.77	6	2.31	6	2.31	....	.....	86	33.08	....	.....	1*o*	0.38	44	16.92
Odessa	Popowski (1)	1921	890	M	515	57.86	480	53.93	3	0.03	....	.....	39	4.38	....	.....	11*o*	1.24	8	0.79
Moscow	Baranovski	1889	1000	n	331	33.10	53	5.30	80	8.0	....	.....	101	10.1	....		26*a* 11*o*	3.16	89	8.90
St. Petersburg	Grechaninoff	1890	583	n	337	57.80	154	26.41	64	10.98	....	.....	218	37.39	....	.....	......	.....	4	0.68

Percentages are based on total number of persons examined (1) = 292 men, 417 women, 181 children examined.

Abbreviations used: *a* = *Taenia saginata*, C = children, M = mixed, n = no data given, *o* = *Taenia solium*.

to the social position, the habits, and the chance relations of the individual. On the other hand a general relation in frequency characterizes a given region in comparison with other areas. Such relations vary with different types of parasites and with different age periods in the life of the host. Tables 1, 2 and 3 are composite records of the work of many investigators, and if analyzed further, would yield many minor relations between the degree of parasitism in different parts of the world and social groupings, racial customs, or climatic conditions. But their main purpose here is to illustrate the degree of infection with helminthes manifested by children and adutls. Despite their incompleteness and certain minor discrepancies they give a fair general picture of that relation. Detailed references to the conditions tabulated are given under the various headings in the text of this article.

Occurrence in Children.—Inadequate attention has been paid to the parasites of children and the data regarding them are still very incomplete. Some species which infect the adult human host are known to be absent in the child, and *vice versa.* In so far as this has been worked out the facts are assembled under the subsequent headings, but other species, known in the adult host and not yet recognized as significant for children, may on further study prove to be present and of importance. I therefore call attention to the need of accurate records by pediatricians on this phase of the subject.

The frequency of parasites in children of different ages has scarcely been investigated and the scant data are difficult to compare. Table 4 shows that the age groups utilized are not uniform and that equally numerous records are not available for all parasites. Furthermore each record covers a selected group either in its geographic location or its social environment and racial origin. In view of these factors, the wide discrepancies in the ratios of infection are not surprising. For Trichuris the table contains 18 records with a range of infection varying from less than 0.2 of one per cent. to 81 per cent. For Ascaris 17 records show a range of infection from less than 0.3 of one per cent. to over 91 per cent. For Oxyuris 13 records give a range of infection from about 0.3 of one per cent. to over 18 per cent. For hookworms the nine records used vary from over one per cent. to 84.5 per cent. *Hymenolepis nana* as recorded in nine investigations was found in from less than 0.5 of one per cent. to 33 per cent. of hosts examined. For Taenia eight investigations show a range of infection varying from 0.1 of one per cent. to over three per cent. The records for *Strongyloides stercoralis* are too few and our knowledge of the parasite too scanty to make any analysis profitable.

From these reports it appears that the most abundant parasites of children are Ascaris and Trichuris with an average frequency as given of over 27 per cent. On the face of the records hookworms are more frequent as the average is over 32 per cent., but the records are fewer and less widely distributed. The third nematode, Oxyuris, has an average frequency of over five per cent. This is surpassed by *Hymenolepis nana* with a frequency record of ten per cent. on the average.

TABLE 4.—AGE INCIDENCE OF VERMINOUS PARISITES IN CHILDREN

Parasites	Ascaris lumbricoides																
Ages	McLean	Greil	DuBuys and Dwyer	Haughwout and Horrilleno	Judkins	Schloss	de Faria	Garrison, Leynes and Llmas	Mendoza-Guason	Stitt	Soulie and Derrieu	Paes	Wilson	Harle, Sutterlin and Zeiss	Araujo	Murphy	da Matta
Under 1 yr.	0	27	0	2	—	—	432	39	10	37	—	91	15	18	238	—	822
1-2	0		0	7	—	—			28		—				977	—	
2-3	0		2	9	—	—		87	32		45					2	
3-4	2		4	6	—	8			39						1,415		
4-5	1		3	5	—			0	43								
5-6	0		5	5	—			119	—	25			0	107			
6-7	0		0	6	42				—		—		71		1,868		
7-8	1		5	4		0			—		—						
8-9	0		7	1		0			—		—						
9-10	0		4	4		0		0	—		—						
10-11	0		6	2		0		50	—	—	—			154	—		
11-12	0		5	4		0			—	—	—				—		
12-13	—	—	5	1		—	—		—	—	—				—	—	—
13-14	—	—	5	—		—	—		—	—	—				—	—	—
14-15	—	—	3	—		—	—	—	—	—	—	—			—	—	—
15-20	—	—	—	—		—	—	—	—	—	—	—		20	—	—	—
Total children infected 15 or under	4	27	*86	56	†42	8	432	295	152	62	45	91	86	279	4,498	2	822
Total children examined	308	665	595	100	15,000	310	1,238	967	1,000	69	316	503	499	878	4,911	102	1,850

0 = Some examined, no parasites found.
— = No persons of that age examined.
* = In the records of DuBuys and Dwyer there are 32 cases of Ascaris, in children for which ages are not given. These have been added to make the total number of children infected.
† = Children of 6–18 years of age.

TABLE 4.—AGE INCIDENCE OF VERMINOUS PARASITES IN CHILDREN.—(*Continued*)

Parasites	Oxyuris vermicularis												
Ages	McLean	Greil	DuBuys and Dwyer	Judkins	Schloss	de Faria	Garrison, Leynes and Llamas	Mendoza-Guason	Soulie and Derrieu	Paes	Harle, Sutterlin and Zeiss	Frey	da Matta
Under 1 yr.	0	5	0	—	—	1	1	0	—	11	8	No age data given all children 16	340
1-2	0		0	—	—			0	—				
2-3	0		1	—	—		1	1	11				
3-4	1		0	—	31			3					
4-5	1		3	—			0	0					
5-6	0		1	—			1	—			50		
6-7	1		3	561				—	—				
7-8	1		2					—	—				
8-9	0		4					—	—				
9-10	0		1				0	—	—				
10-11	0		0				0	—	—		63		
11-12	0		1		0			—	—				
12-13	—	—	2		—	—		—	—				—
13-14	—	—	1		—	—		—	—				—
14-15	—	—	3		—	—	—	—	—	—			—
15-20	—	—	—		—	—	—	—	—	—	7		—
Total children infected 15 or under	4	5	*37	†561	31	11	3	4	11	11	121	16	340
Total children examined	308	665	595	15,000	310	1,238	967	1,000	376	503	878	270	1,850

0 = Some examined, no parasites found.
— = No persons of that age examined.
* = In the records of DuBuys and Dwyer there are 15 cases of Oxyuris, in children for which ages are not given. These have been added to make the total number of children infected.
† = Children 6–18 years of age.

TABLE 4.—AGE INCIDENCE OF VERMINOUS PARASITES IN CHILDREN.—(*Continued*)

Parasites	Trichuris trichiura																	
Ages	Greil	DuBuys and Dwyer	Haughwout and Horrilleno	Judkins	Schloss	de Faria	Garrison Leynes and Llamas	Mendoza-Guason	Stitt	Soulie and Derrieu	Paes	Harle, Sutterlin and Zeiss	Araujo	Murphy	Frey	da Matta	Stiles and Garrison	Crowell and Hammack
Under 1 yr.	5	0	2	—	—	446	22	3	28	—	225	4	132	—	No age data given all children 6	896	16	18
1–2		0	5	—	—			4		—			843	—				
2–3		1	9	—	—		75	8		77			1,289	4				
3–4		4	9	—	33			12										
4–5		6	10	—			0	15										
5–6		1	5	—			108	—	23			42						
6–7		8	6	28				—		—			1,711					
7–8		6	7					—		—								
8–9		18	3					—		—								
9–10		15	4				0	—		—								
10–11		16	3				44	—	—	—		34	—					
11–12		19	4					—	—	—			—					
12–13	—	16	2		—	—		—	—	—			—	—		—		
13–14	—	13	—		—	—		—	—	—			—	—		—		
14–15	—	7	—		—	—	—	—	—	—	—		—	—		—		
15–20	—	—	—		—	—	—	—	—	—	—	1	—	—		—	—	—
Total children infected 15 or under...	5	†201	69	†28	33	446	249	42	51	77	225	81	3,975	4	6	896	16	18
Total children examined............	665	595	100	15,000	310	1,238	967	1,000	69	316	503	878	4,911	102	270	1,850	123	116

0 = Some examined, no parasites found.
— = No persons of that age examined.
* = In the records of DuBuys and Dwyer there are 71 cases of Trichuris, in children for which ages are not given. These have been added to make the total number of children infected.
† = Children 6–18 years of age.

TABLE 4.—AGE INCIDENCE OF VERMINOUS PARASITES IN CHILDREN.—(*Continued*)

Parasites	Hookworms									Strongyloides stercoralis			
Ages	Greil	DuBuys and Dwyer	Haughwout and Horrilleno	Judkins	de Faria	Garrison, Leynes and Llamas	Araujo	Frey	da Matta	DuBuys and Dwyer	Judkins	de Faria	Garrison, Leynes and Llamas
Under 1 yr.	177	0	0	—	120	0	114	No age data given all children 155	1,270	0	—	58	0
1–2		0	0	—			819			0	—		
2–3		0	0	—		1				1	—		2
3–4		1	1	—			1,391			0	—		
4–5		0	0	—		0				1	—		0
5–6		0	0	—		4				0	—		1
6–7		0	3	3,844			1,830			1	4		
7–8		1	1							3			
8–9		0	3							1			
9–10		1	2			0				3			0
10–11		0	0			11	—			4			0
11–12		1	1				—			2			
12–13	—	1	1		—		—		—	3		—	
13–14	—	3	—		—		—		—	3		—	
14–15	—	0	—		—	—	—		—	1		—	—
15–20	—	—	—		—	—	—		—	—		—	—
Total children infected 15 or under	177	*16	12	†3,844	120	16	4,154	155	1,270	*38	†4	58	3
Total children examined	665	595	100	15,000	1,238	967	4,911	270	1,850	595	15,000	1,238	967

0 = Some examined, no parasites found.
— = No persons of that age examined.
* = In the records of DuBuys and Dwyer there are 8 cases of Hookworms, 15 cases of Stronglyloides in children for which ages are not given. These have been added to make the total number of children infected.
† = Children 6–18 years of age.

TABLE 4.—AGE INCIDENCE OF VERMINOUS PARASITES IN CHILDREN.—(*Continued*)

Parasites	Hymenolepis nana									Taenia								Other parasites			
Ages	Greil	DuBuys and Dwyer	Judkins	Schloss	Soulie and Derrieu	Paes	Frey	Stiles and Garrison	Machado	Judkins	Schloss	de Faria	Mendoza-Guason	Harle, Sutterlin and Zeiss	Murphy	Frey	Schiodte	(1) Haughwort and Horrilleno	(2) Judkins	(3) Murphy	(4) Greenway
Under 1 yr.	38	0	—	—	—	0	No age data given all children 90	6	—	—	—	22	1	3	—	No age data given child 1	No age data given all children 43	135	—	—	13
1–2		0	—	—	—	1			—	—	—		0		1				—	—	
2–3		0	—	—	64	3			—	—	—		0						—	1	
3–4		4	—	20		3			—	—	5		0						—		
4–5		1	—			6			—	—			0						—		277
5–6		3	—			1			—	—			—	13					—		
6–7		1	71		—	4			—	69			—						60		
7–8		1			—	7			—				—								
8–9		2			—	5			2				—								
9–10		1			—	0			2				—								
10–11		0			—	2			2				—	10							
11–12		5			—	0			1				—								
12–13	—	5		—	—	1			0		—	—	—		—					—	
13–14	—	2		—	—	—			1		—	—	—		—			—		—	
14–15	—	5		—	—	—			1		—	—	—		—			—		—	—
15–20	—	—		—	—	—		—	—		—	—	—	4	—			—		—	—
Total children infected 15 or under..	38*	55	†71	20	64	33	90	6	9	†69	5	22	1	26	1	1	43	135	60	1	290
Total children examined..............	665	595	15,000	310	316	503	270	123	300	15,000	310	1,238	1,000	878	102	270	9,000	100	15,000	102	2,470

0 = Some examined, no parasites found.
— = No persons of that age examined.
* = In the records of DuBuys and Dwyer there are 25 cases of Hymenolepis all in children for which ages are not given. These have been added to make the total number of children infected.
† = Children 6–18 years of age.
(1), (2), (3) = Protozoan findings; (4), Hyadtid cysts.

Probably this average will be raised as attention is more carefully directed to this species. The average frequency of Taenia is only about one per cent. In some cases a frequency of zero should no doubt be entered for parasites with fewer records, but certain investigators were especially concerned with particular species of parasites and no final conclusion can be drawn from failure to mention any other parasites.

EFFECTS OF PARASITIC INFECTIONS

Historical.—Throughout antiquity and up to 200 years ago, general opinion, even of the medical profession, assigned some sort of parasite to every disease, real or imaginary. Each complaint was believed to have its particular worm in a characteristic location. Such views have been abandoned and, in general, writings of more recent times have assigned less and less importance to parasitic species until opinions have reached the opposite extreme of considering parasites entirely devoid of pathologic significance. The reaction from this view has already set in, but even today the physician tends to minimize the effects of parasites while the public tends to exaggerate them.

Direct Effects.—Usually internal parasites are present in limited numbers and are regarded as harmless when few or of small size. Naturally the effect of a minute parasite is small and difficult to measure. Nevertheless, even such an effect is a tax on the host, and the tax increases in proportion to the number, size and habits of the parasites present. It makes a wide difference, moreover, whether the parasite is inactive or actually growing, although even encysted parasites exert pressure on adjacent parts. If a growing parasite is located in proximity to important structures, they may become seriously involved and the pressure give rise to irritation in these tissues, occlude indispensable blood-vessels or press dangerously upon nerves.

Further, the parasite requires a definite amount of nourishment for its sustenance. This material must be taken directly from the host and comes from what the latter has already secured or elaborated for its own use. Some intestinal parasites live on the food in the lumen of the canal, others on epithelial cells, others on the blood or lymph. The attack on the tissues may be merely mechanical or it may be chemical, by the action of secretions. This draft on the energy of the host makes parasites of serious significance particularly for children.

A small number of parasites when tangled, such as a mass of ascarids in the intestine, may affect the host fatally by occlusion of the canal, or in the blood system a vessel may be closed or a clot produced by the presence of even a single parasite (Fig. 387).

Active parasites give rise to irritation and resultant inflammation of membranes. One observes this effect in maximum in the hookworm, which tears down and consumes the cells of the epithelium, causing continuous and depressing hemorrhage, and since the parasite secretes an anticoagulin, the hemorrhage persists a long time after the worm has left the spot. A few parasites may thus provoke very serious damage.

Other species burrow their way through the tissue, producing not only small hemorrhages but a serious flow of blood when some large vessel chances to be ruptured. The perforation of the lung tissue by migrating larval ascarids gives rise to pneumonic symptoms, and the penetration of the alimentary wall by a single ascaris may induce a fatal peritonitis.

Indirect Effects.—The indirect effects of parasites are on the whole more significant than these direct results. Laceration of the intestinal wall affords points for easy attack of the pathogenic microorganisms in the intestinal contents. The destruction of the tissues, the resultant inflammatory processes, with the replacement of physiologically active cells by scar tissue, and a series of undesirable retrogressive histologic changes, make the indirect results ultimately of even greater significance than the direct mechanical changes.

Toxicity.—A further disturbance induced by parasitic infection is of the most profound significance. It has been shown that various parasites contain toxic materials of specific character which, when extracted and utilized experimentally, affect unfavorably the nervous system and the formation of blood. The continued production and elimination of such substances would explain effects that sometimes seem excessive in parasitic diseases. Reflex nervous symptoms are thought to occur. Cases are reported in which there appeared a meningismus resembling tuberculous meningitis but tubercle bacilli were not found in the cerebrospinal fluid.*

Anemia.—An apparent pernicious anemia results from this toxic stimulation, accompanied by a relatively high mortality in infections with certain species. The mode of production of the toxic material, its relation to normal processes in the parasite, its variability in action in different hosts and at different times are still undecided problems. One cannot doubt, however, that extracts from different species of parasites vary greatly in toxic power. Even from the same species of parasite there have been isolated different toxic principles, one acting on muscles and another on nerve centers, both producing experimentally, when injected into healthy animals, results analogous to those observed in parasitic diseases.

Eosinophilia.—Parasitic infections are very frequently, if not always, associated with a marked eosinophilia, the percentage of which is subject to wide and rapid fluctuations. Eosinophilia is characteristic of other conditions as well as of parasitic infection, though it reaches an extreme in parasitic infections not otherwise observed. Trichinosis, especially in the most serious cases and in those in which there are bacterial complications, may show no eosinophilia. In some cases of infestation with other worms in which the patient is doing very poorly, the absence of eosinophilia is a striking feature. Data on this condition reported by different investigators appear to be contradictory in many instances.

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* Guillain, Georges et Gardin, Ch. Contribution à l'étude des méningites de l'helminthiase. Bull. acad. méd., Mar. 14, 1922, pp. 308–316.

General Conclusions.—Based on their exhaustive study, Haughwout and Horrilleno* state: "We believe that intestinal parasitism, both directly and indirectly, contributes towards the high death-rate in young Filipino children." These and other studies suggest that the personal habits and environment of the children have direct bearing on the frequency of intestinal parasitic infections and, further, that this frequency has a definite effect on both the physical development and the mental progress of school children. Stiles† finds that even light infection with *Ascaris lumbricoides* and *Necator americanus* is a factor in retarding progress in school children. More recent work by Smillie in Alabama throws doubt upon the effects of light infections since it required 100 worms or more to register physical and mental retardation.

SYMPTOMS DUE TO PARASITIC INFECTION

The symptoms commonly regarded as indicative of the presence of parasites are in no sense precise and not even generally dependable. Among such symptoms have been listed frequently: grinding of the teeth, scratching of the nose, disturbances during sleep, ravenous appetite, lassitude, and itching about the buttocks or in the perineal region. No one of these is diagnostic, and even a series of them may be caused by or associated with other conditions. In 102 cases with various diagnoses, admitted consecutively to a children's hospital, examination of the feces by Murphy‡ revealed intestinal parasites in seven cases, the symptoms of which are given in Table 5.

TABLE 5.—COMMON SYMPTOMS IN HELMINTHIASIS

Number	Age	Sex	Race	Nationality	Intercurrent disease	Parasite	Gastrointestinal	Nervous	Loss in weight	Skin
1	6	F	R. J.	U. S.	Chorea	T. t.	Appetite poor	Very nervous		
2	10	M	R. J.	U. S.	Mitral and aortic insufficiency	T. t.	Appetite poor abd. distress	Restless		
3	8	M	R. J.	U. S.	Endocarditis	T. t.				
4	4	M	R. J.	U. S.	Leg burn	Asc. l.				
5	2½	F	R. J.	U. S.	Chronic osteomyelitis	Asc. l.				
6	6	M	R. J.	U. S.	Helminthiasis	Tae. s.	Appetite poor	Slightly	Slight	Purpura hemorrhagica
7	4	M	R. J.	U. S.	Burns	Tri. i.				

* Haughwont, F. G., and Horrilleno, Fe S., The intestinal animal parasites found in one hundred sick Filipino children. Phillipine J. Sc., Manila, xvi (Jan., 1920), pp. 1–75.

† Stiles, C. W., Zooparasitic intestinal infections; an analysis of infections found among 1287 school children (776 white, 511 negro) of the city of X. Pub. Health Rep., Washington, xxx (1915), pp. 1991–2002; Recent studies on school children, with special reference to hookworm disease and sanitation. New York M. J., (1915), p. 906.

‡ Murphy, W. W., Helminthiasis in children. Am. J. Dis. Child., iv (Dec., 1912), p. 379.

One is indeed not justified in looking for a symptom complex diagnostic of all parasitic worm infections. The worms differ in precise location, in food and method of feeding, in body secretions and waste products, in physical and physiologic activities—in short, in all vital manifestations. Hence the problem is individualistic and it is essential to determine the symptom complex for each species as a basis for diagnosis. De Buys and Dwyer,* who examined the stools of 600 children in seven institutions, emphasize rightly the inadequacy for diagnosis of general symptoms and the importance of demonstrating either the parasites or their ova before subjecting patients, especially small children, to anthelmintic therapy.

Confusion of Symptoms.—Emphasis should be laid on two further features: (1) intestinal parasites are frequently the cause of undiagnosed maladies in children, and (2) certain cases of intestinal parasites in children are readily confused with other diseases, such as typhoid fever, appendicitis and acute infection of the gall-bladder. These cases emphasize the need of careful exclusion of parasitic infection before radical procedure for other complaints is begun.

DIAGNOSIS OF HELMINTHIC INFECTIONS

The precise determination of a parasitic worm is a matter of primary importance. The life history, manner of infection, effect on the human host, and method for removal are characteristic of each particular species, and the purpose of the physician has often been defeated by failure to have accurate knowledge of the worm involved. Precise diagnosis is important here as elsewhere, and equally clearly related to prognosis and prophylaxis.

In reaching a definite conclusion as to the type of worm involved it is necessary to consider three questions:

1. What types of worms occur as parasites and which of these are found in the human host?
2. What methods can be utilized to determine the actual presence of suspected "worms" and to secure material as a basis for diagnosis?
3. How are the materials obtained to be utilized in an accurate differentiation of the species involved? An important element here is the consideration of pitfalls in diagnosis.

These questions will be discussed briefly under the following headings: *Classification of Parasites, Materials for Diagnosis, Methods of Differentiation,* and *Pseudoparasites.*

Classification of Parasites.—It was long believed that animal parasites constituted a discrete group which could be classified separately from other types of animal life, but it is now recognized that parasitic species are merely specialized forms of free-living organisms. In consequence, the classification of parasites reduces itself to a location of parasitic species in the general classification.

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* De Buys, L. R., and Dwyer, H. L., Study of the stools in children's institutions showing the incidence of intestinal parasitic infections. Am. J. Dis. Child., xviii (Oct., 1919), p. 269.

Protozoa and Metazoa.—Two major subdivisions of animal types are at present universally recognized, the Protozoa or single-celled animals, and the Metazoa or many-celled. They may be differentiated on the basis of size and of general appearance. The Protozoa are all minute and most of them are too small to be seen by the unaided eye. They can be detected only with the microscope, and their study involves considerable knowledge of microscopic technique and experience in the interpretation of such delicate objects. The Metazoa are large and of sufficient size to be readily visible. Some of the smallest flukes or mites are only a fraction of a millimeter in length, but most of the Metazoa are conspicuous objects, and the big tapeworms or roundworms are from one to many meters in length.

While zoologists recognize in the animal kingdom some 10 to 16 phyla or major branches, only a few of these are significant from the standpoint of helminthology, *viz.*, the Plathelminthes or flatworms and the Nemathelminthes or roundworms.

The Plathelminthes.—Among the Plathelminthes, the Trematoda or flukes are consistently parasitic species, although in certain developmental stages they are free-swimming and carry infection from one host to another. The Cestoda or tapeworms are exclusively parasitic also, with very few instances of a free-swimming larval stage; and in the adult stage are well-known and striking parasites of the vertebrates.

The Nemathelminthes.—The roundworms contain three classes which display very little similarity in structure although commonly associated in a single phylum or branch as a matter of convenience. (1) The Nematoda or true round- or threadworms include both free and parasitic species and are common in all types of environment. The parasitic species are usually larger than the free-living species. (2) The group of Gordiacea contains slender, filamentous forms, popularly known as hair snakes. These organisms pass their early life as parasites in insects and the adult stage free-living in fresh water. (3) Acanthocephala, or thorny-headed worms, are exclusively parasitic in habit and highly specialized for this mode of existence. As human parasites they are so rare as to be practically unknown.

Leeches and Arthropods.—Two other small groups contain certain characteristic parasites. These are the leeches among the annelids and some of the Arthropoda (insects and mites). They are not treated in this article.

Terminology.—One notes occasional criticism by medical men of the complex terminology and changes in names employed by zoologists for parasitic species. The names of parasites are not changed from caprice but from necessity. In fact, part of the trouble is due to the failure of medical men to consider the technical character of animal nomenclature and to seek expert advice from zoologists. The subject is most complex; it has been worked out after long discussion by technically trained men. The Rules of the International Congress govern, and the law of priority holds.

Today is the day of the specialist in all sciences, and confusion will be avoided as well as greater progress achieved through consultation and cooperative research by investigators in both fields.

The following is a list of the human parasites discussed in this article:

SYNOPSIS

TREMATODA

Suborder	Family	Sub family	Genus and species
Distomata	Fasciolidae	Fasciolinae	Fasciola hepatica
			gigantica
		Fasciolopsinae	Fasciolopsis buski
	Echinostomatidae	Echinostomatinae	Echinostoma
			ilocanum
			Euparyphium
			malayanum
			jassyense
	Dicrocoeliidae	Dicrocoeliinae	Dicrocoelium
			lanceatum
	Heterophyidae		Heterophyes
			heterophyes
			nocens
			Metagonimus
			yokogawai
	Troglotrematidae		Paragonimus ringeri
			westermani
			kellicotti
	Opisthorchiidae	Opisthorchiinae	Opisthorchis
			felineus
			viverrini
			Clonorchis sinensis
			endemicus
	Schistosomatidae	Schistosomatinae	Schistosoma
			haematobium
			japonicum
			mansoni
			bovis

SYNOPSIS

CESTODA

Order	Family	Sub family	Genus and species
Cyclophyllidea	Taeniidae	Taeniinae	Taenia saginata
			solium
			confusa
			marginata
			serrata
			crassicollis
			infantis
			coenurus
			Echinococcus
			granulosus
			multilocularis
	Hymenolepididae	Hymenolepidinae	Hymenolepis nana
			fraterna
			diminuta
	Dipylidiidae	Dipylidiinae	Dipylidium
			caninum
	Davaineidae	Davaineinae	Davainea
			madagascariensis
			asiatica
			formosana
	Anoplocephalidae	Anoplocephalinae	Bertiella satyri
Pseudophyllidea	Diphyllobothriidae	Diphyllobothriinae	Diphyllobothrium
			latum
			cordatum
			parvum
			americanum
			mansoni
			Sparganum
			proliferum
			Diplogonoporus
			grandis
			brauni
			Brauni jassyensis

SYNOPSIS

NEMATODA

Order	Family	Sub family	Genus and species
Anguilluloidea	Anguillulidae	Rhabditinae	Rhabditis niellyi
			hominis
			Heterodera radicicola
	Angiostomidae		Strongyloides stercoralis
	Gnathostomidae	Gnathostominae	Gnathostoma spinigerum
			hispidum
Filarioidea	Filariidae	Filariinae	Filaria bancrofti
			conjunctivae
			ozzardi
			tucumana
			hominis-oris
			Agamofilaria georgiana
			Acanthocheilonema perstans
		Onchocercinae	Dirofilaria magalhaesi
			Loa loa
			Onchocerca volvulus
			caecutiens
	Dracunculidae	Dracunculinae	Dracunculus medinensis
Spiruroidea	Spiruridae	Gongyloneminae	Gongylonema pulchrum
			scutatum
			subtile
		Spirurinae	Habronema sp.
			Physaloptera caucasica
			mordens
	Thelaziidae		Thelazia callipaeda
	Mermithidae		Agamomermis hominis-oris
Dioctophymoidea	Dioctophymidae	Dioctophyminae	Dioctophyme renale
Trichenelloidea	Trichinellidae	Trichurinae	Trichuris trichiura
			Hepaticola hepatica
		Trichinellinae	Trichinella spiralis
Strongyloidea	Ancylostomidae	Ancylostominae	Ancylostoma duodenale
			Necator americanus
			Ancylostoma braziliense
			Necator suillus

SYNOPSIS.—(*Continued*)

NEMATODA

Order	Family	Sub Family	Genus and species
Strongyloidea	Strongylidae	Strongylinae	Oesophagostoma brumpti stephanostomum Ternidens deminutus
	Syngamidae		Syngamus laryngaeus
	Trichostrongylidae	Trichostrongylinae	Trichostrongylus colubriformis orientalis probolurus vitrinus Mecistocirrus fordi Haemonchus contortus
	Metastrongylidae	Metastrongylinae	Metastrongylus apri
Ascaroidea	Ascaridae	Ascarinae	Ascaris lumbricoides maritima Belascaris cati Toxocara canis
	Oxyuridae	Oxyurinae	Oxyuris vermicularis
		Syphaciinae	Syphacia obvelata

Materials for Diagnosis.—Evidence of the actual presence of parasites is obtained by the examination of the sputum, urine, blood and feces. The first three are frequently studied but rarely yield any evidence of parasitic infection. The feces are much less often examined and frequently only superficially, although they furnish the most material for accurate diagnosis. Although little employed even today, the importance of fecal examination was demonstrated some 200 years ago. In an early attempt to classify children's diseases by the nature and appearance of the stools, John Astruc* in 1746 devoted especial attention to parasitic worms. He maintained as the result of his observations that worms do not arise spontaneously, as was generally believed at that date, but that they are produced from eggs.

The careful macroscopic and microscopic examination of fecal discharges may result in the discovery of entire worms or of fragments. The larger worms and the tapeworm joints are usually seen by the naked eye and promptly determined, although not always with desirable accuracy. But there are small species of both tapeworms and threadworms that are often overlooked, and the minute larvæ of nematodes as well as the ova of all worms can be detected only by precise microscopic examination. In the study of fresh feces several mounts should be made from each stool; even then mild infections will be overlooked. For greater accuracy as well as ease in this study, various methods of concentration are used, since the minute size of some parasites and of all larvae and ova renders their detection difficult when the amount of other material is large.

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* Abt, Isaac A., History of the classification of gastro-intestinal diseases in ancient and modern times. Am. J. Dis. Child., iv (Aug., 1912), p. 68.

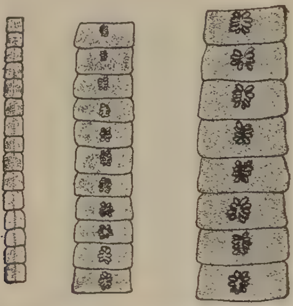

FIG. 345.—Parts of chain of Broad Tapeworm *Diphyllobothrium latum*. Natural size. (After Braun.)

Flotation Method.—Among the many methods devised for handling feces to demonstrate the ova of helminths the best is the brine flotation method of Kofoid and Barber as modified by Fülleborn:*

In a glass of about 200 c.c. capacity are placed 1 part of feces (normal consistency) and 20 parts of concentrated salt solution, and the mixture stirred or shaken to an even consistency. The glass should be filled about 7 or 8 cm. high. In this mixture the eggs rise rapidly to the surface, where the greatest number appear in from half to three-quarters of an hour. After several hours they disappear from the surface. Not only Ancylostoma, Necator and Trichostrongylus eggs, but also Ascaris eggs, can be examined by this method. Ascaris eggs rise

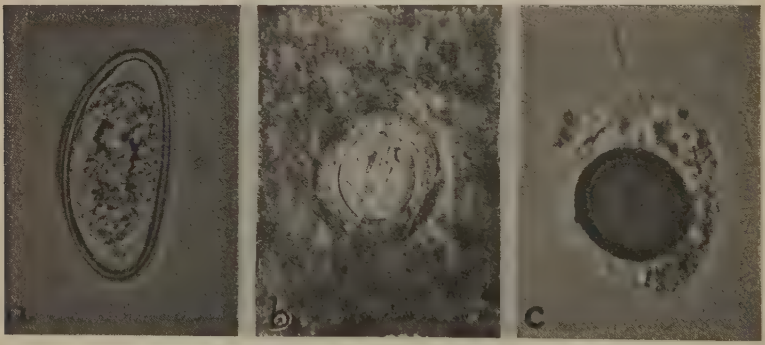

FIG. 346.—*a*, *Oxyuris vermicularis*, from fresh stool; *b*, *Hymenolepsis nana*, from fresh stool; *c*, *Taenia saginata*, from *very* fresh stool. (All figures photomicrographs by Dr. T. B. Magath.) ×500.

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* Fülleborn, F., Die Anreicherung der Helmintheier mit Kochsalzlösung. Deutsche med. Wchnschr., xlvi (June 24, 1920), p. 714.

more slowly to the surface than Ancylostome eggs, so that even after one hour or more an examination may give negative results.

The method is excellent for the eggs of *Hymenolepis nana*, whereas the eggs of *Hymenolepis diminuta* sink again after three-quarters of an hour. *Taenia saginata* and Oxyuris eggs can also be searched for by this method, although Telemann's* method may prove better. The method is not applicable to Bothriocephalus or trematode eggs, nor to stronglyloid larvae. Fülleborn did not find it successful for Amoeba or Lamblia cysts but it proved very satisfactory for Coccidia cysts.

The Centrifuge Method.—This method is preferred by many. No salt solution is employed. A tube containing diluted and strained feces is subjected to rotation in the centrifuge until the ova are thrown to the bottom, when the process must be stopped. The rate of speed and the time must be determined by experiment, and the personal equation is larger than in the brine flotation method, but in the hands of an experienced observer the centrifuge method is very satisfactory.

Härle, Sütterlin and Zeiss state that Fülleborn's concentration method with sodium chloride yielded positive results in 26 per cent. of cases negative by the ordinary methods of fecal examination.

Differentiation of Larvae.—In the determination of species from the material obtained, one should remember that the small size and simple structure tend to make these worms look much alike. Careful comparison of details with a good description is always essential. While this is true of adult parasites, it is still more so of the larvæ, since in the early stages many organs of adult structure are lacking. The determination of the nematode larvæ, like those of the hookworm and of Strongyloides, demands most accurate work. Data for differentiating the species in both the larval and the adult stages are given in the subsequent pages under the appropriate headings. The ova, however, appear most frequently; they differ in some general features.

Trematode Ova.—The egg of the trematode is oval, rarely spherical or irregular, with a smooth surface save for a single process or spine in a few cases. The shell is moderately thick and varies from light to dark brown, with corresponding differences in transparency. Within the shell is either a cell mass or a developing embryo. In the latter case a globule of reserve material can be distinguished beside the embryo. At one end the shell possesses a cap or lid often difficult to see, which opens when the egg is ripe to permit the escape of the embryo or miracidium. The latter is covered by cilia but has no hooks. Often they may be differentiated by size or form, but sometimes the texture of the living egg affords the only safe criterion for diagnosis (Fig. 347).

Cestode Ova.—The cestode egg is surrounded by a series of three membranes of which the middle one is thick and cross-striated in characteristic manner. Only in the fish tapeworm among human cestodes does the shell open by a lid to allow the escape of the six-hooked larva. This spherical larva, the oncosphere, is characteristic of the tapeworm, but is so small it is often not seen.

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* Telemann, Walter, 1908, Eine Methode zur Erleichterung der Auffindung von Parasiteneiern in den Feces. Deutsche med. Wchnschr., xxxiv(August 27, 1908) pp. 1510–1511.

Nematode Ova.—The nematode egg varies much in shape, from an oval or spindle to a sphere, and in degree of development when laid. The single shell is usually colorless. It varies from a tenuous membrane to a heavy cover that may have an outside deposit of considerable thickness. The egg content may be a single cell or a fully developed embryo, or any intermediate stage.

Variation in Ova.—In a given mass of eggs there are likely to be some stunted or abnormal forms. Hence, average measurements should be taken from a series of normal specimens, and all ova that are distorted or exceptional should be rejected. Although all ova in a given species are fairly similar, one must expect some differences.

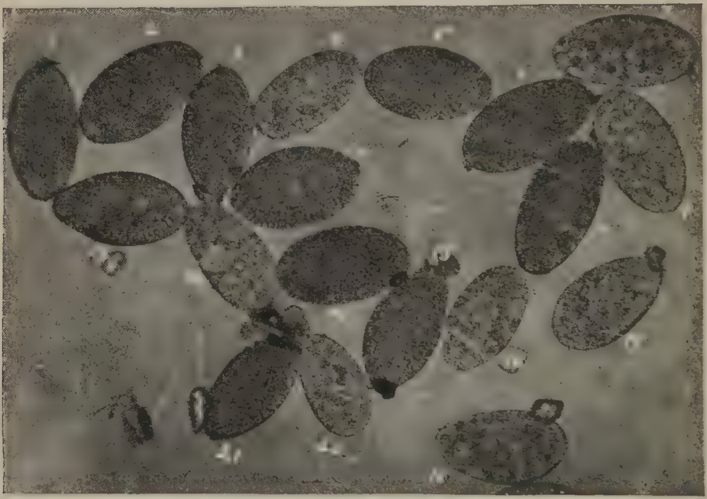

Fig. 347.—Ova of *Fasciola hepatica* and *Fasciolopis buski*. Magnified. (Photo by courtesy of Dr. C. H. Barlow.)

Pseudoparasites.—In the search for the cause of some obscure malady or in the routine examination of materials, the diagnostician often sees specimens which are said to be of parasitic nature and the cause of the troubles under consideration. The examination and evaluation of such materials must proceed with extreme care. The determination of parasites is not easily made, and it is not a simple matter to distinguish between true parasites and other materials. Some of the pitfalls have entrapped many confident and even careful observers.

Source of Material Examined.—At the outset it is essential to establish beyond possible doubt the true source of the materials in question. To be sure, the deceitful introduction of curious objects that are subsequently displayed as having come from the body of the patient is not generally to be feared in the case of children, although it is a frequent and difficult situation to contend with among malingerers and certain nervous types. Even with children, it is not impossible that a nurse, parent, or other person of peculiar mentality may secretly introduce extraneous material into a container or force it into the body to be evacuated at stool. Therefore all statements regarding the source of reputed parasites must be scrutinized most rigidly.

Character of the Material.—Once it is established that the material actually emanated from the patient, equal difficulties arise in determining its character and source. Inexperienced observers are often powerfully impressed by peculiar bodies in the feces which come to view under the microscope. Many of the objects are recognized by the trained microscopist as non-pathogenic. For diagnostic purposes it is important that the physician be able to recognize such objects just as accurately as those which are actual causes of disease. In general these extraneous and irrelevant objects have been classed as pseudoparasites, although they differ widely and have in common only the fact that, by virtue of one factor or another, they simulate true parasites. Keeping in mind the frequency with which such things occur, the diagnostician should examine any new material with the distinct feeling that deception is unconsciously or unintentionally likely to be practiced, and should constantly endeavor to explain unusual objects otherwise than as parasites.

Supposititious Parasites.—Pseudoparasites may be grouped under a series of different headings. The first of these embraces real animals, usually living and often even of the same general type as parasitic species, but only apparently parasitic in man. A fish nematode taken from a hollow tooth proved, in fact, to be in no way a parasite of man. It was accidentally ingested with food and mechanically forced into the tooth. Small roundworms from stomach contents were nothing but specimens from the soil in which grew the onions that had been eaten in such great abundance as to cause pronounced gastric difficulties. The worms had no etiologic significance whatever. The "hair snake," a roundworm which as an adult lives free in moist soil or water, has frequently been recovered from the human body. However, it is in the adult stage a free-living species, and its presence in man during that period is much more unfortunate for the worm than for its host, because it can neither work damage nor even continue to exist in such location. Yet it has been blamed for most serious difficulties. Its presence in the vomit of a child was undoubtedly due to the fact that it was eaten by chance in an apple or other fruit, or else was picked up from the ground and swallowed accidentally, an occurrence recorded among adults and common with children. Indeed the child's well-known habit of experimenting with possible food materials will readily explain the presence of such things in the stomach. Careless consumption of over-ripe fruit or partly spoiled food materials would readily account for the presence in the human system of fly maggots, beetle larvæ, grubs of various moths, etc. Very heavy-skinned varieties, such as the thousand-legged worms, can resist digestion long enough to be carried unharmed entirely through the canal. They may be detected in the feces, and the unusual character of the discovery give rise to the view that these species are the cause of the trouble under consideration. In a most baffling case the ova of a free-living nematode were ingested with uncooked green vegetables and diagnosed after detection in the feces as the eggs of an unknown human parasite which was designated in the literature as *Oxyuris incognita* (*vid. infra*).

Unrelated Objects.—In contrast with living animals of the type just noted, the second group of pseudoparasites includes structures which, though described as parasites, are incapable of assuming such a rôle, and in fact, are entirely unrelated to parasitic species. Thus fragments of the human body itself have been frequently described as parasites. Fragments of the hyaloid artery have been frequently designated as eye worms, and small axillary glands and hydatid moles appear periodically in the literature as hydatid cysts.

Food.—Partially digested food substances simulate parasites in some cases in a very striking manner, and this type of pseudoparasite is most likely to be found in children because of the slow or imperfect action of digestive processes. Seeds, plant vessels and undigested fragments of tissue are frequently taken for intestinal worms, and even have been described and baptized as such. Various authors have repeated the account of partially digested banana fibers which closely simulate minute tapeworms. The partly digested pulp vesicles of an orange bear a striking resemblance to small flattened trematodes. Imperfectly digested strips of cabbage cut on a slicing board produce, when partly digested, rather perfect imitations of certain tapeworms.

Extraneous Objects.—In all of these cases, the structures come naturally from the body of the patient, and, in most instances are modified by it to resemble some normal parasite. There are, however, many extraneous objects that at times are diagnosed as parasites. Dusting powders used for infants frequently contain lycopodium spores which, appearing in the urine or feces, have been diagnosed as the eggs of parasites. Normal free-living organisms, such as rotifers, have been discovered and reported as new species of parasites from urine because they were present by accident in the container. An indigenous case of "filariasis" was described from Devonshire because the blood films were contaminated by cotton fibers. Peculiar hookworms on further study proved to be plant hairs. Spherules of leucine in the urine were regarded as eggs of the giant kidney worm. A piece of peach skin with its plant hairs, which had been coughed up by a patient was reported as a hydatid cyst of the lung with characteristic hooks on the membrane. And the list might be indefinitely extended.

Differentiation.—In the long run, even the most confusing objects can be diagnosed, but a hasty or superficial examination is sure to lead to difficulties. All nonpathologic objects must be carefully discriminated and eliminated from consideration if the true parasitic organisms are to be properly determined. In general an artifact is inert, whereas a true living organism possesses distinct and independent movement. A partly digested fragment of tissue possesses a roughened, inexact outline, in sharp contrast with the clear, well-defined boundaries of a living organism. But the eye of the experienced microscopist becomes so familiar with these and other features as to have a firm basis for distinguishing promptly between the true and the false.

ANTHELMINTICS*

Principles.—An anthelmintic is a drug used to kill or to remove intestinal worms. Often the worms are not killed but stupefied, they being removed by the normal action of the intestine or the administration of a laxative or cathartic. A vermicide is a drug which kills parasitic worms and a vermifuge is a drug used to remove but not to kill intestinal worms. As the subject is inadequately studied, this distinction cannot be applied with certainty in most cases. Most drugs now used, seem to exert in part both effects in individual cases. It is obvious that an efficient anthelmintic must act more deleteriously on the parasite than the host and to this end more investigation is necessary since most of the drugs used at the present time are toxic to the patient, especially to children. In dosing children with such dangerous drugs as anthelmintics a high degree of professional and individual judgment, training and experience is absolutely essential.

Anthelmintics have been shown to possess little if any specific effect on parasites and thus to prevent extreme toxic effect on the host it is necessary to provide for the rapid expulsion of the drug by the patient. The use of drugs that are absorbed slowly also aids in preventing poisoning. The dosage of the anthelmintic, unlike other drugs, should be on the basis of the effect on the worms and not on the age of the patient, except in so far as the gross area of the intestinal tract of the child differs from that of the adult, and the question of dilution must be considered. Usually it is necessary to reduce the adult dose for children.

Treatment.—In general five steps in the treatment of intestinal worms should be very carefully carried out, preferably in a hospital or at least with the cooperation of very intelligent parents.

1. Preparation. In general this consists in starving the patient for a period of at least three meals over a 24 hour period. Then a large enema should be given. It is often wise to give a small dose of Epsom salts at the beginning of the starvation period.

2. Administration of the drug. This is usually done in broken doses, but if the drug causes vomiting it must be given by stomach tube.

3. Purgation. After a varying length of time depending on the drug, a brisk purge should be given. Since many of the anthelmintics

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* In preparation of this section on Anthelmintics valuable aid has been given by Dr. M. C. Hall, of Washington, D. C. and Dr. T. B. Magath of Rochester, Minn.

are soluble in oils, purges containing oil should be avoided. Castor oil is an exception to this rule. As a rule a saline cathartic is safest.

4. Enema. About two hours after the administration of the purge, or at the time when the patient feels that the bowels are going to move, an enema of clear water should be given and the bowel movement passed directly into the container in which the stool is to be examined.

5. Examination of the stool. It is important to determine exactly the results of the treatment. In the case of tapeworms the head should be found, and after treatment for flukes and round worms, the worms should be obtained. Not all may come away at one time and it is always wise and important to examine the stool of the patient sometime after treatment to make sure that all the parasites have been removed. The time which should elapse before the second examination varies with the worm; for example, in the case of *T. saginata*, one should wait at least a month in order that egg-producing segments may develop.

Necessity for Drugs.—"Therapeutic nihilism in the field of anthelmintics has little to sustain it. While the drugs used in this capacity are in need of much more study, they nevertheless include a number of demonstrably potent drugs serving a purpose that cannot be served by any means other than medicinal, except by way of prophylaxis . . . Anthelmintics are selective in action, at least their dependable effectiveness is limited to certain sorts of worms . . . The anthelmintic activity of a drug is not proportional to its antiseptic properties . . . Suitable modes of medication are often demanded for individual drugs . . . Passage of worms is indication for repeating or continuing rather than stopping the treatment . . . Severe helminthiasis should be treated with caution. [The patient weakened by long illness has increased susceptibility to the toxic properties of drugs]. . . . While the majority of worms pass out the first day, many come from one to seven days afterward."*

Specific Drugs.—While the physician must be governed to some extent by the conditions under which he is working, the type of patient and the degree and type of infestation, in general the following drugs will answer as an adequate list. Under each drug is indicated the type of worm most generally treated and the form of administration. Fuller details are given under individual headings for various parasites.

1. Santoninum. Usually combined with calomel when administered to children. It is used almost exclusively to remove Ascaris. It should be given only in repeated small doses.

2. Aspidium. Best used in emulsion form with powdered acacia and water. The oleoresin is the usual form of the drug. This anthelmintic is very efficient for the removal of tapeworms.

3. Oil of chenopodium. The oil of the American wormseed has been used in recent years and is a very efficient remedy for hookworms. It is thought to be equally efficient against Ascaris and perhaps other intestinal worms, and is more valuable in a single dose than santonin. It may be given on sugar lumps or in capsules.

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* Hall, M. C., A discussion of some principles of anthelmintic medication. New Orleans M. & S. J., cxx (February, 1918), pp. 637–653.

4. Carbon tetrachloride. Especially used in the treatment of hookworms. The dose being small it is best to administer it in hard capsules. It has been used with some success in the treatment of whip-worms. For mixed infection with hookworms and Ascarids the best treatment known is a mixture of chenopodium or ascaridol and carbon tetrachloride.

5. Thymol. This classical treatment for hookworms is usually given to children in 0.5 to 1.0 gm. doses. It is repeated in two hours and given every day for a week. Castor oil must not be given either before or after thymol treatments.

6. Antimony, in the form of either sodium or potassium antimony tartrate (the sodium salt is said to be less toxic than the potassium salt) in given intravenously, either alone or alternating with arsphenamine. It is used in cases of filariasis, schistosomiasis and dracontiasis.

7. Emetine hydrochloride is an alternative for antimony and in many cases the drug of choice in schistosomiasis.

I. TREMATODA

General Data.—The flukes are parasitic flatworms in which the body is made up of a single region. They are distinguishable from the related tapeworms by the form of the body and by the presence of an alimentary canal. None of these worms occur regularly as human parasites on the North American continent, and even among the introduced species there are none as yet reported for children. In other parts of the world, however, endemic forms cause serious diseases, some of them particularly in children. Introduced species at first are found in hosts who have brought the parasites with them from other countries; thus the imported parasites which are occasionally observed in North America are found in adults who have traveled, not in children, whose movements are more limited. But with the growing freedom of movement between different parts of the world, foreign species of parasites are likely to be introduced often, and if they find favorable conditions, to establish themselves. They may then become in North America, as in their former habitats, of especial significance to children, rather than to adults. For that reason, several species demand consideration even though they have not yet been reported from North America.

Adult Anatomy.—Trematoda are bilaterally symmetrical worms, usually somewhat elongated and flattened, and only rarely cylindrical or somewhat thickened and shortened, so as to approximate an ovoid or spheroid in outline. The body is without an internal cavity and consists in large part of parenchymatous tissue filling in all the spaces between the organ systems. At the anterior end is usually a sucker which opens into the alimentary system, and the majority of the common species possess also a sucker on the ventral surface; this is not connected with any other organ.

The simple alimentary canal is sac-like, usually having the form of a tuning fork, with only a single opening, the mouth, which is surrounded by the oral sucker. Just behind this on the esophagus is a powerful sphincter, the pharynx. The excretory system is of the protonephridial type, being composed of a branching series of fine tubules, ultimately closed by stellate flame cells. The excretory pore lies at or near the posterior end.

The reproductive organs are for the most part exceedingly complex and constitute the mass of the body. These worms are, with rare exceptions, hermaphroditic. The general arrangement of the reproductive system may be seen from Fig. 348.

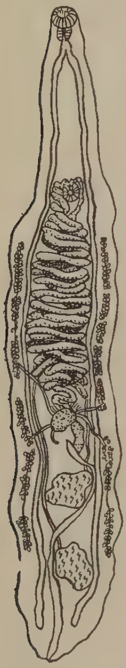

FIG. 348.—Typical Distome. *Opisthorchis pseudofelineus.* Original figure. ×5.

Male Organs.—Although the two systems are closely associated, the male system is nowhere connected with the female save at the common genital pore. Immediately inside this pore is a genital cloaca into which empty the terminal ducts of both systems. The testes, usually two in number, are compact round or oval bodies connected each with a fine tube, the vas efferens, which unites with its fellow from the other testis to form the vas deferens. Usually this enters, near the genital pore, a complex which contains a seminal vesicle, a muscular organ, the cirrus, and a sac, though any and indeed all of these parts may be wanting. This group of structures is usually conspicuous and aids in the diagnosis of species.

Female Organs.—The female system starts with the ovary, a compact mass, round or oval in most cases. The oviduct leading away from this organ is met by a transverse vitelline duct, which carries the secretion of the highly developed lateral vitelline glands and has in some cases a distinct median yolk reservoir. Around the oviduct lies a delicate structure known ordinarily as the shell gland or better Mehlis' gland. The shell-forming material comes probably from the large lateral vitellaria, and Mehlis' gland delivers probably a precipitin or coagulin that functions in the formation of the egg-shell. From the fertilization space, where oviduct and yolkduct meet in Mehlis' gland, a tortuous slender tube leads to the genital cloaca. This tube, the uterus, varies greatly in length and is ordinarily crowded full of eggs. In some species a conspicuous sac, the receptaculum seminis, lies near the fertilization space and is related to a fine tube, Laurer's canal, which rises almost directly to the dorsal surface and opens by a minute pore. One or both of these structures may be lacking.

Life Cycle.—The number of eggs produced is very large, and the variations in the life history between different species are conspicuous. In most instances the development is complex, involving one or more changes of host and an alternation of generations. Ordinarily the eggs, discharged from the parent worm into some cavity in the body of the host, ultimately reach the exterior, and within the shell there develops a ciliated embryo, which embraces the first suitable opportunity to escape, *i.e.*, when by chance the egg is brought into a pool or other body of water. Once set free, the ciliated embryo or miracidium swims about, seeking eagerly for the intermediate host (Fig. 349). This is not of the species which was host to the adult, but regularly, and nearly always, a mollusk of a particular type. Having gained entrance into the body of this host, the embryo changes into a sac (sporocyst) in which is produced usually a different brood (redia). But in the blood-flukes daughter sporocysts are produced. Within the redia there arises later a new generation known as the cercariæ (Fig. 350). By virtue of a powerful swimming tail a cercaria, after having deserted its host, moves about vigorously through the water in which it may ultimately encyst; it may bore its way in actively or passively be swallowed by, and encyst in, a second host (Figs. 351, 352). This is the stage in which the infection of the final host takes place. When by chance the encysted form is engulfed by a proper host, the cyst is lost and the larva becomes free to seek its proper location; here it grows into the adult worm and gives rise to a new generation of eggs. Marked differences in detail exist between the species.

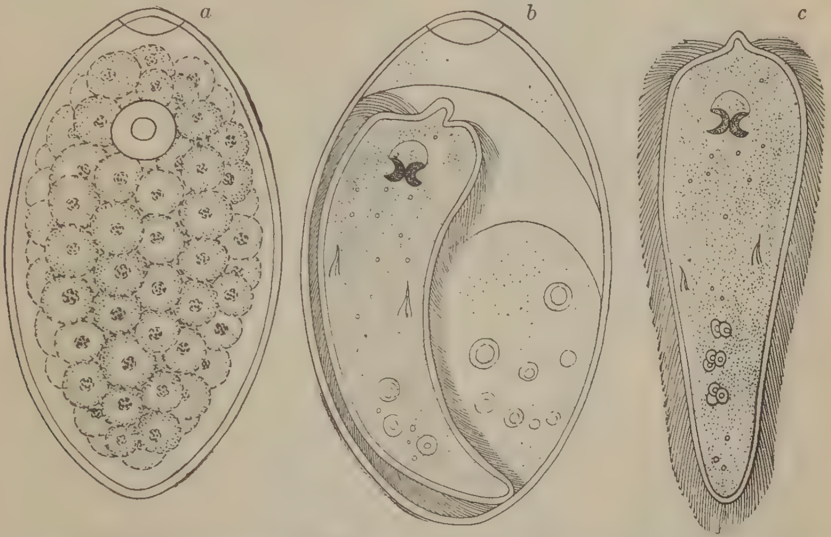

Fig. 349.—Development of distome. *Fasciolopsis buski*. *a*, undeveloped egg; *b*, fully grown miracidium in eggshell; *c*, free swimming miracidium. ×500. (After Nakagawa.)

TREMATODES RECORDED AS HUMAN PARASITES

FAMILY FASCIOLIDÆ Railliet 1895
GENUS FASCIOLA Linnaeus 1758

Diagnosis.—Large distomes with leaf-shaped body, anterior conical projection, large and powerful acetabulum. Small dermal scales. Esophagus short, pharynx present, intestinal crura near median line, extending to posterior end, provided on median side with short projections and on lateral aspect with long branching pockets. Excretory system much branched, with long median spindle-shaped reservoir. Genital pore median, pre-acetabular. Ovary anterior to transverse yolk duct, lateral, branched. Testes, one on each side, posterior to transverse yolk duct, dendritic. Uterus in form of rosette, anterior to germ glands. Vitellaria lateral, highly developed, in cortical zone, extending from acetabulum to posterior end. Laurer's canal present, receptaculum lacking. Eggs large, not abundant; development begins after deposition.

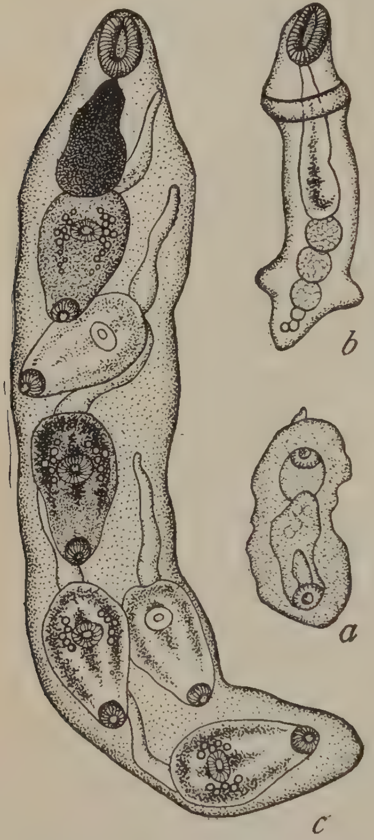

Fig. 350.—Development of distome. *Fasciolopsis buski.* *a*, sporocyst stage; *b*, immature redia; *c*, fully grown redia enclosing cercariæ. *a*, *b* ×90; *c*, ×120. After Nakagawa.)

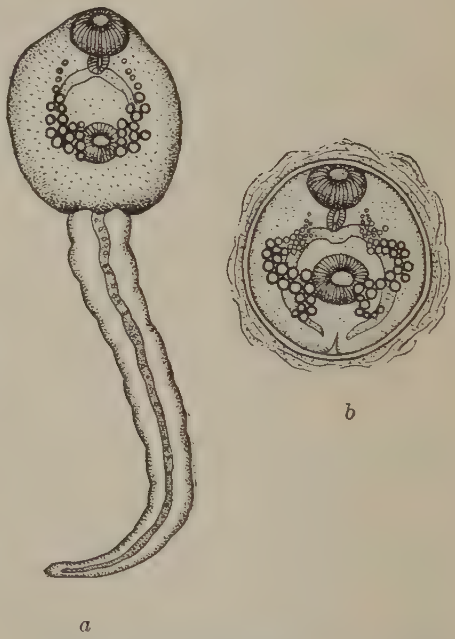

Fig. 351.—Development of distome. *Fasciolopsis buski.* *a*, mature cercaria, ×120; *b*, encysted agamic distome, ×170. (After Nakagawa.)

Fasciola hepatica Linnaeus 1758

Synonyms.—*Distomum hepaticum* Retzius 1786; *Fasciola humana* Gmelin 1790; *Distomum caviae* Sonsino 1890; *Cladocoelium hepaticum* Stossich 1892.

Description.—This exceedingly common European parasite of sheep, which occurs also frequently in other herbivores, has a length of from 20 to 30 mm. with a breadth of from 8 to 13 mm. The anterior cone, from 4 to 5 mm. long, is rather sharply set off from the main part of the body. The hemispherical suckers are conspicuous and measure, for the oral sucker 1 mm., for the ventral 1.6 mm. in diameter. The intestine forks half way between these suckers, and the branching of the crura is rich and conspicuous. The eggs are yellow-brown, oval, provided with a cap, and measure 130 to 145μ in length and but 70 to 90μ in breadth.

Distribution.—The parasite is distributed widely over Europe and has been introduced into North America. Records of *F. hepatica* from other continents sometimes indicate confusion with closely related species. In the domestic animals, especially in sheep, the parasite gives rise to an inflammation of the liver which attains the significance of an epidemic and works great damage in the flocks. The disease breaks out towards the end of summer and is especially severe in the winter. Even those sheep which recover suffer serious, permanent injury. Erratic specimens of these parasites occur in the lungs and rarely in other tissues, but the liver is their proper seat.

Life Cycle.—The eggs distributed with the droppings of the sheep develop when by chance they reach water. From the egg comes the ciliated elongated larva (miracidium), which seeks out a snail; in Europe this is *Limnaeus truncatulus* Müll. In this new host the miracidium becomes a sporocyst within which are developed young of a new generation, differing slightly in structure from the sporocyst and designated as rediæ. At times these produce a new generation like themselves, or again a generation of individuals of a different type known as cercariæ. The latter are free living and at the appropriate time make their way out from the snail to lead a brief active existence in the open water, after which the animal encysts on a blade of grass or other solid object. It may even form a cyst on the surface film of the water, and in this event may be carried about indefinitely by wind and currents. The infection of the new primary host occurs when this cyst is swallowed with food or drink. Ordinarily this host will be some herbivorous domestic animal, but circumstances may bring the cyst into the human stomach, where it is opened by the action of the gastric juice and the young worm emerges, migrates to the liver, and enters on an active period of growth to the adult form. The percentage of infected domestic animals in Europe is high, although in recent years it has been much reduced through various preventive measures.

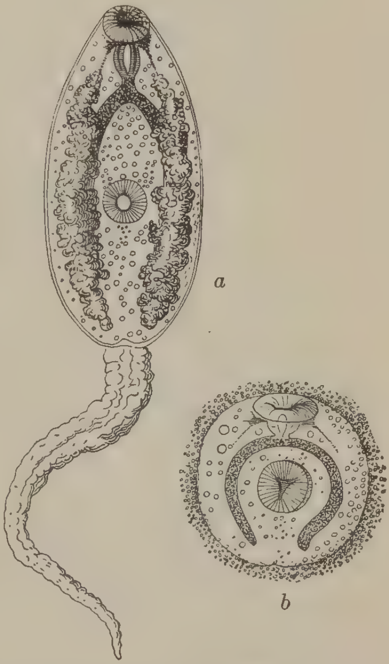

Fig. 352.—*Fasciola hepatica.* *a*, free swimming cercaria; *b*, agamic distome encysted. Magnified. (After Leuckart.)

Occurrence in Man.—So far as man is concerned, the sheep liver fluke is only an occasional parasite which enters the human system by chance and in such scanty numbers that it arouses no special symptoms. Most of the cases have been demonstrated at necropsy or by the discovery of the eggs in fecal examinations. In some cases no symptoms were detected in advance; in others, severe complications were noted; in one case death resulted. The symptoms are generally referable to the liver. The diagnosis is made from eggs in the feces.

The sheep liver fluke is one of the rarest of human parasites in the Western World. It has been reported from children only once in the 50 human cases on record. According to some writers, it is commonly met with as a human parasite in Tonkin, and occurs there probably both in children and adults. The young, encysted distome enters the human body accidentally with contaminated water and uncooked foods, salads, water cress, etc.

One of the two cases recorded from children* comes from the University clinic at Tübingen and is noteworthy in that it was diagnosed *intra vitam.* Fecal examinations disclosed numerous eggs of *Fasciola hepatica* in September and November, 1920, and again in November, 1921, in a girl of eight years, who enjoyed good health during this period.

Treatment of Liver Fluke.—**Prophylactic.**—Vogel suggests that children should not be employed—as often is done—to collect from sheep pastures snails of the intermediate host of the fluke. The danger of infection is great when they handle these shells and unwittingly transfer to the mouth the young fluke cysts adhering to the fingers.

Medicinal.—There is no specific treatment. Children should be kept away from sources of infection and given a wholesome diet, good air and proper exercise. The complement-fixation test of Fairley and Williams† for hepatic distomatosis in sheep may some day be useful for man to test the therapeutic effect of such drugs as urotropin, helmitol and salicylates, which are excreted in bile and can be administered intravenously.

Fasciola gigantica (Cobbold 1858)

This species, closely related to the common European sheep liver fluke, may be differentiated from it by the greatly elongated body, short anterior cone, and almost parallel lateral margins. The eggs are also larger, measuring from 150 to 190μ in length and from 75 to 90μ in breadth.

Very few cases are on record, and these are reported for adults. The parasite is an African species though reported from man in South

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* Vogel, R., Ueber das intra vitam beobachtete Vorkommen des grossen Leberegels (Fasciola hepatica L.) bei einem Kinde. Centralbl. f. Bakteriol., 1. Abt., (Jena, 1921–22), Orig., lxxxvii (Jan. 31, 1922), p. 556.

† Fairley, N. H., and Williams, F. E., Observations on the complement fixation reactions in liver fluke (*Fasciola hepatica*, L.) infection. J. Path. and Bacteriol., xxvi (Jan., 1923), p. 19.

America, and more frequent cases, involving children as well as adults, may be looked for on the African continent.

GENUS FASCIOLOPSIS Looss, 1899

Body elongate oval, without oral cone. Acetabulum, with deep cavity extending posteriad, projecting, much larger than oral sucker. Prepharynx and pharynx conspicuous. Intestinal crura separate almost immediately behind pharynx and extend to posterior end; not branched but sinuate. Vitellaria extensive, lateral, reaching almost entire length, follicles minute, in surface layer. Mehlis' gland in center of body. Ovary small, branching, and dextral. Uterus with scanty coils. in anterior region. Testes coarsely branched, filling posterior region; cirrus sac long, conspicuous, enclosing spiral, tubular seminal vesicle. Genital pore pre-acetabular.

Fasciolopsis buski (Lankester 1857)

Synonyms.—*Distomum buski* Lankester 1857; *Distomum crassum* Cobbold 1860; *Opisthorchis buski* R. Blanchard 1895; *Distomum rathouisi* Poirier 1887; *Fasciolopsis goddardi* Ward 1909; *Fasciolopsis fülleborni* Rodenwaldt 1909; *Fasciolopsis spinifera* Brown 1917.

This worm is thick and opaque as well as very irregular and variable. The length is from 24 to 37 mm., the breadth from 6 to 12 mm. The body is linguiform; the dermal spines are caducous. The oral sucker measures 0.5 mm. in diameter, the acetabulum 2.5 mm. The pharynx is spherical, 0.7 mm. in diameter. The esophagus is hardly 0.25 mm. long. The intestinal crura have three or four shallow curves. The cirrus sac extends about one-fourth the entire body-length. The testes are entirely posterior to the transverse yolk ducts; the ovary is mostly anterior but has a few branches posterior. The vitellaria are confluent at the posterior end. The eggs measure from 120 to 130μ in length and from 70 to 80μ in breadth (Fig. 353).

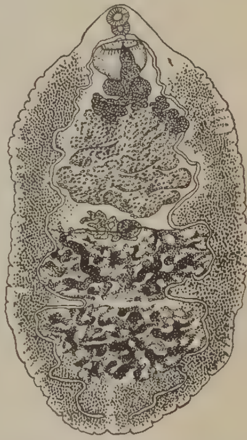

FIG. 353.—*Fasciolopsis buski.* Adult, magnified about 2½. Original figure.

Distribution.—This species is parasitic in man, and possibly in the pig, but Barlow could not find a single case of pig infection in a region where the parasite was very abundant in the human host. In Fukien he found the parasites often in pigs but not once in man. The species inhabits the duodenum primarily, though it is found in adjacent portions of the canal but "never in the bile duct." It is very abundant in Shaohsing, and is found from Borneo and the Malay peninsula through South China as far north as the Yangtse River. Maxwell reports it in Formosa.

The species was discovered in London in 1843, at the necropsy of a Lascar sailor. In 1873 Dr. Joseph Leidy described two cases in Canton, China, from material sent him by J. G. Kerr. One of these cases was in a 15 year old Chinese boy. Later a Siamese boy in Bangkok passed specimens carefully described by Odhner, to whom we owe an exact knowledge of the structure and systematic position of the parasite. A specimen found at necropsy is reported from Galveston, Texas.

Life History.—The oval yellow-brown eggs occur abundantly in stools, and are distinguished with difficulty from those of *Fasciola* *hepatica* (Fig. 347). Measurements of eggs differ widely according to various authors: 130 to 140μ by 80 to 85μ (Goddard); 120 to 130μ (Faust); 120 to 138μ by 70 to 95μ (Brown) and 99 to 181μ by 43 to 120μ (Barlow). Thanks to Barlow, the life history of Fasciolopsis (Figs. 349–351) is well worked out. When feces containing ova are deposited in water, the eggs hatch in from 25 to 38 days. The miracidium, which possesses an X-shaped eyespot, swims about actively in the water and seeks out snails; according to Barlow a Planorbis and a Segmentina of unidentified species serve as larval hosts. Attacking the epithelium of the snail, the miracidium penetrates into subdermal lymph spaces, and in the process loses bit by bit its ectodermal covering. The simple transformation into a sporocyst is followed by the development of germ cells, visible even in the miracidium near the posterior end, into rediæ. When the rediæ are mature they desert the sporocyst and migrate through lymph spaces to the pericardial sinus and liver. Here daughter rediæ are produced from germ cells that live in the posterior portion of the body cavity of the first generation. Barlow states that the formation of a second generation of rediæ is a constant feature of the life history. The daughter rediæ are distinguishable from the first generation of rediæ by their much greater size, less developed musculature, smaller locomotor organs, and narrower intestine. From germ cells in the posterior end of the body cavity, they produce cercariæ, which appear in from 25 to 35 days after the entrance of the miracidia into the snail. These cercariæ emerge into lymph spaces and after several days make their exit from the snail near the line of contact between the mantle and the shell. They swim about in the water for short distances and encyst on plants or other convenient objects.

Such a cercaria measures almost 1 mm. in length, of which the body includes 0.16 to 0.35 mm., with a width of 0.15 mm. and the tail 0.72 to 0.74 mm. with a width of 0.06 mm. It possesses an oral sucker, a pharynx, and an esophagus which gives rise to two simple ceca just anterior to the ventral sucker. Two flame cells near the middle of the body and two groups of cystogenous glands are conspicuous structural features. The cyst wall is thick, transparent and very tough, but the cercariæ cannot resist drying. One finds cysts abundantly on the water-caltrop and water-nut. In one area every nut was infected, 18 cysts being the average and 40 the most taken from a single fruit. These nuts are eaten raw by the Chinese. The ingested cysts are not affected by gastric digestion, but rupture in the duodenum, where the young fluke develops into an adult. The period of development from adult fluke to adult fluke is 91 days or more, depending on temperature and moisture.

Incidence among Children.—The parasite is very common among children and its eradication is evidently a matter of great difficulty, as it is almost impossible to keep raw food out of their mouths. It occurs in 7.5 per cent. or more of all dispensary patients; in one set of 304 fecal examinations, 28 per cent. showed infection. The clinical picture includes (1) a period of latency: few flukes, no trouble except lowered resistance; (2) a period of diarrhea: stool light yellow, very offensive, much undigested matter; in children, very protuberant abdomen, and (3) a period of edema; most distressing, anemia very marked; abdominal cavity first affected, then genitals, legs and finally arms, face and lungs; dyspnea due to ascites may require paracentesis every five or six days (Fig. 354).

A slight infection produces mild symptoms; the patient complains of a dull griping hypogastric pain, and an eosinophilia of from 8 to 10 per cent. is noted. When the flukes are abundant the pain becomes more severe, like that of gastric ulcer, and subsides on taking food. Diarrhea and constipation alternate, and edema is nearly always noted. Nausea and vomiting accompany heavy infection, with general asthenia and anasarca. Death is due to toxemia.

Treatment.—For these parasites Noc finds thymol in the usual doses very effective. As an anthelmintic for *F. buski*, Barlow prefers carbon tetrachloride to betanaphthol, because the former is less irritating in action and its effects pass away more quickly.

Fasciolopsis rathouisi (Poirier 1887) was originally described from a single specimen voided by a native in Shanghai and sent to France. Odhner who examined the same specimen in 1909 concluded that it was only a badly contracted specimen of *F. buski*. Other workers have described as new species, material from China and Siam under the names *F. goddardi*, *F. fülleborni*, *F. spinifera*. Continued studies favor the view that these all belong to one species *F. buski* which is subject to extreme changes in form under different conditions.

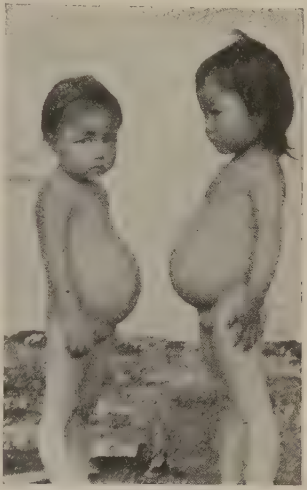
FIG. 354.—Chinese children infected with Fasciolopsis. (Photo by courtesy of Dr. C. H. Barlow.)

FAMILY ECHINOSTOMIDÆ Looss 1902

Diagnosis.—Elongate distomes with powerful acetabulum near anterior end; oral sucker weak, surrounded at anterior end of body by collar or ruff open on ventral surface, and bearing one or two rows of strong, straight spines. Ventral spines sometimes conspicuously heavier than the others. Genera and species determined largely by numbers and arrangement of spines. Body generally spinous and muscular. Eggs are large, thin-shelled.

Garrison found one species, *Echinostoma ilocanum*, in five cases, in the Philippines and Leiper another species, *Euparyphium malayanum*, in two cases from Singapore and vicinity. A third species, *Euparyphium jassyense*, has been described by Leon and Ciurea from Jassy, Roumania; the host was a Russian. All three instances represent only occasional parasites of man, and in the first two cases at least, the normal hosts are native mammals. A fourth species of similar character is *Echinochasmus japonicus*.

Case in a Child.—All of the records for the foregoing three species concern adults, but children are even more likely than adults to pick up adventitious parasites. One case which is probably due to the second species noted in this family, but which was originally attributed to a new species designated *Artyfechinostomum sufrartyfex* Clayton Lane 1915, was reported from India. This species has 39 spines on the collar, two of which are large terminal spines. The parasites were passed by a native girl aged eight, in Assam, who died shortly thereafter of general debility.

FAMILY DICROCOELIDÆ Odhner 1911

The common lancet fluke of the sheep, *Dicrocoelium lanceatum* Stiles and Hassell 1896, is recorded in eight cases as a human parasite in Europe. The limited number of such cases, coupled with the marked abundance of the parasite in European sheep indicates clearly the existence of some condition (mechanical?) that militates against the infection of man.

FAMILY HETEROPHYIDÆ Odhner 1914

In this family one species, *Heterophyes heterophyes*, (Fig. 355) was discovered in Egypt by Bilharz in 1851 in the intestine of a boy. In recent years Looss has shown that it is frequent but usually overlooked because of its minuteness. The worms occur in the middle third of the small intestine, and in the midst of food masses, not on the wall of the intestine, so that Looss regards them as harmless even when present in large numbers. The species occurs in dogs and, rarely, in cats. Young distomes, found by Khalil encysted in the mullet from Lake Menzalch and fed to cats, developed into the adult *H. heterophyes;* so that evidently man may acquire this parasite by eating poorly cooked fish. The species, originally discovered in a child and common in Egyptian children, is said by Looss to be of no pathologic significance. It is most frequent in rural districts and rare or entirely wanting in city residents and in Europeans in Egypt. The records from Japan are attributed to a second species, *Heterophyes nocens* Onji and Nishio 1915, common in certain parts of that country but this may be the same as the Egyptian species.

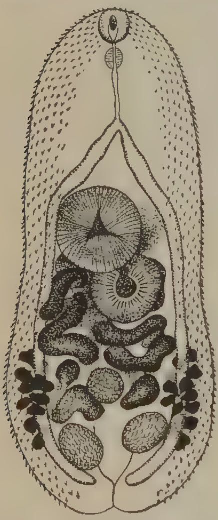

FIG. 355.—*Heterophyes heterophyes.* Ventral view, magnified. (After Looss.)

Another closely related form is *Metagonimus yokogawai* (Kobayashi 1912) (Syn.: *Metagonimus ovatus*) reported from man in Japan in 1913 by Yokogawa. It lives in the small intestine of man and dog. In Formosa and also in certain interior districts of central, southern, and western Japan it is not uncommon. In an extreme case more than 4000 worms were evacuated by a single host in response to anthelmintic treatment. Life history studies are said to show that the encysted larva is found on the exterior and also in the subcutaneous connective tissue and superficial muscles of a fresh-water salmonoid (*Plecoglossus altivelis* Temm.). Since the flesh of the fish is sliced thin and eaten raw as a delicacy, it is easy to see how man becomes infected. The species is limited in its range and not likely to spread or become endemic even if transferred to other countries. Unlike the preceding species, this one burrows in the mucosa and destroys the glands of the intestinal wall. In consequence it possesses distinct pathologic importance.

FAMILY TROGLOTREMATIDÆ Odhner 1914

Body more or less flattened, compressed, with high arched dorsum. Skin thickly spined. Cirrus sac wanting. Ovary pretesticular, lobed. Vitellaria richly developed in dorsal cortical zone. In pairs in cysts.

GENUS PARAGONIMUS M. Braun 1899

Distomes with thick body, almost circular in cross-section. Suckers well separated. Pharynx spherical; crura unbranched, much crenated, extending to posterior end. Excretory bladder long, irregular in caliber, pore slightly ventral. Genital pore postacetabular, inconspicuous; no cirrus sac. Testes deeply lobed, lateral, in posterior region. Ovary also deeply lobed, lateral, near center of body, balanced by short, tighly coiled uterus on other side. Vitellaria lateral and dorsal in cortical zone. Eggs large thin-shelled.

Paragonimus ringeri (Cobbold 1880)

Synonyms.—*Distoma ringeri* Cobbold 1880; *Distoma pulmonis* Kiyona, Suga and Yamagata 1881; *Distoma pulmonale* Baelz 1885.

Body plump, ovate, reddish brown in life with ventral surface flattened. Length 5 to 12 mm., breadth 4.5 to 7 mm.; thickness 3.5 to 5.5 mm. Suckers nearly equal in size, 0.75 to 0.9 mm. in diameter; oral sucker subterminal, ventral sucker anterior to center of body. Skin with chisel-shaped scales arranged in groups. Excretory bladder long, widest near center of length, with numerous lateral branches. Amphitypy or situs inversus common. Genital pore just behind acetabulum, slightly lateral. Seminal vesicle thin-walled, sacculate, inconspicuous. Testes not extensive. Ovary about equal in size and similar in branching. Eggs thin shelled, brownish, 81 to 87μ long and 49 to 51μ broad.

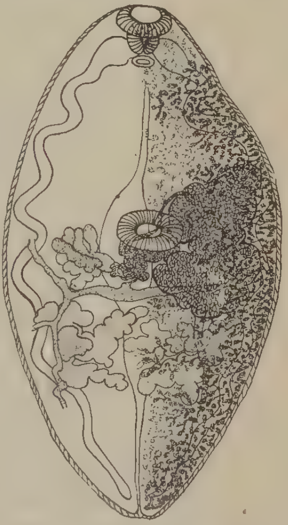

FIG. 356.—*Paragonimus kellicotti*. Vitellaria drawn on right side only. Original drawing ×4. (After Ward and Hirsch.)

The species *Paragonimus westermani*, first discovered in 1878 by Kerbert in Amsterdam in the lungs of a tiger, differs, according to Ward and Hirsch,* from the form found in man in Japan and Formosa and described originally by Manson and Cobbold. In the dog, cat and pig in North America, Ward, Stiles, and others have described a closely related form that is regarded as a third species, *Paragonimus kellicotti* (Fig. 356). Outside of Japan where, Katsurada states, no districts are entirely free from this parasite, it occurs frequently in Formosa, Korea, certain parts of China, and the Philippines. Imported specimens have been found in Europe, Africa, and North America, and recently in Peru and Yucatan; the exact species found in each region is uncertain.

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* Ward, H. B. and E. F. Hirsch, The Species of Paragonimus and Their Differentiation. Ann. Trop. Med. and Parasitol., ix (March, 1915) pp. 103–162.

Life History.—The development of the human lung fluke has been fairly well worked out by Japanese investigators. In cultures kept at about 30°C., the eggs produce a ciliated miracidium in from 25 to 35 days. In Formosa Nakagawa found stages in two snails, *Melania libertina* and *M. obliquegranosa*, and also described the cercaria. Encysted distomes occur in fresh water crabs, the cysts in the liver being half grown and those in the gills fully developed. In Japan Yoshida demonstrated that three species of river crab were infected: *Sesarma dehaanii* (Milne Edwards), in the lower reaches of the streams, not used for food; *Eriocheir japonicus* (de Haan), the fur crab, an edible crab but always cooked before eaten; and *Potamon dehaanii* (White), the pond crab, in shallow waters of mountain streams, eaten both raw and cooked.

TABLE 6.—INFECTION WITH HUMAN LUNG FLUKE IN DIFFERENT LOCALITIES; WITH CRAB SPECIES FUNCTIONING AS SECOND INTERMEDIATE HOSTS

SPECIES OF CRAB	COUNTRY	PROVINCE
Potamon obtusipes (Stimpson)............	Formosa	Shinchiku
Potamon dehaanii (White)...............	Formosa	Shinchiku
Potamon dehaanii (White)...............	Japan (?)	Nigata, Gifu
Eriocheir japonicus de Haan.............	Formosa	Okayama
Eriocheir japonicus......................	Japan	Shinchiku
Eriocheir japanicus......................	Korea	Tokushima, Okayama
Sesarma dehaanii (Milne-Edwards).......	Japan	Osaka
Sesarma dehaanii not infected in	Formosa	Shinchiku
Astacus japonicus (de Haan).............	Korea	
Potamon sinensis (Milne-Edwards).......	Formosa	Taihoku

The degree of infection varies widely in different localities, but in general in the order given in Table 6, and the crab species named function as the second intermediate hosts according to Kobayashi, Ando and Nakagawa. Yoshida has shown that the cysts become loosened from the gills and drift about in the water, so that infection is evidently due in part to contaminated drinking water.

Kittens and puppies were experimentally infected, and the infection of children is doubtless easy and frequent. Nakagawa reached the conclusion, however, that eating crabs infected with cercariæ is the chief cause of the disease in Formosa, as 77 per cent. of patients suffering from the disease gave a history of eating hairy crabs and 14 per cent. had eaten red crabs, or a total of 91 per cent. in all.

Incidence among Children.—The human lung fluke gives rise to pulmonary disease (parasitic hemoptysis) especially frequent in mountainous regions of Japan, China, Formosa, and Korea. Here it is limited to the intermediate river valleys, and absent near the coast as well as in the turbulent waters of the upper rivers. In some villages, human infection is as high as 82 per cent. Kakami records that in Korea, 25 per cent. of those examined below 10 years of age were infected, and 57 per cent. of those between 10 and 20; among savages in North Formosa 50 per cent. are infected, as also 4.3 per cent. of pupils in all the public schools. The infection persists for long periods (from 10 to 20 years), and is of greater significance among adults because of economic considerations. But in many cases this infection is acquired in childhood. It is, however, infrequent in girls in Korea in the first three decades of life, according to Ogi. Nearly all persons infected are farmers or in the families of farmers, and commonly several in the same family are infected.

Symptoms.—Aberrant worms have been recorded from many parts of the body and are most dangerous in the brain, where, in one case at least, the parasite led to the formation of a fatal brain tumor in a lad. Among children in Formosa, Korea and Japan, many cases of *Paragonimus ringeri* are associated with brain invasion. Earlier these cases were diagnosed as cerebral infantile paralysis, cerebral hemorrhage, encephalitis, or acute meningitis. In these regions the inhabitants show a high incidence of infection with *Paragonimus ringeri*, and among the infected children symptoms of focal cerebral disease were frequent. In young animals infected experimentally, the parasite had penetrated the cervical veins. Accordingly, Kawamura, Ishibara and Yamaguchi, who studied the cases, thought it probable that the same method of invasion occurred among children. In two small towns were found 37 cases in children, of which 11 were between 6 and 10 years old, and 18 between 11 and 15 years. The onset of the disease was at from three to five years in six cases, at from 6 to 10 years in 20 cases, and the great majority had acquired the disease before the age of 15. The symptoms are severe headache with vomiting and dizziness, often epileptic attacks, at times of the Jacksonian type, and rarely aphasia and loss of sight. The symptoms observed at the onset of the disease disappear gradually for the most part, but persist in some cases. The mentality of the patients is weakened and some die of brain complications. In these regions, when the streams are low in summer, the children play in the water, catch the crabs and eat the viscera raw or half boiled. Encysted distomes are found in from 24 to 100 per cent. of the crabs examined in these places.*

Treatment.—According to Brumpt treatment is purely symptomatic although it is likely that emetine can be used with success. Vegetables, uncooked fish, unboiled water and shell-fish enter largely into the diet of classes to which infected persons chiefly belong; thus the preventive measures are self-evident. The use of surface water for drinking, washing or even bathing will serve to introduce the abundant floating cysts. Field workers and above all children are thus liable to acquire infection accidentally.

FAMILY OPISTHORCHIIDÆ Braun 1901

Long, much flattened, transparent distomes with delicate muscles and weak suckers. Intestinal crura extend to posterior end. Excretory bladder Y-shaped with short branches and long stem. Neither cirrus nor cirrus sac. Germ glands in posterior region. Uterus long; transverse coils between ovary and acetabulum. Eggs very numerous, small, asymmetrical.

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* Kawamura, R., and Yamaguchi, M., On the Pulmonary Distomiasis which Caused Brain Symptoms in Children. Japan Med. World, i (Aug. 15, 1921) pp. 11–7.

GENUS OPISTHORCHIS R. Blanchard 1895

Body somewhat pointed at anterior end and rounded posteriorly. Suckers relatively close together. Pharynx present, esophagus short, crura long, simple. Excretory bladder Y-shaped, with long stem curving between testes in form of an S. Genital pore pre-acetabular. Testes posterior, oblique, lobed. Ovary median, pretesticular, receptaculum large, just behind ovary. Vitellaria lateral, restricted, with small follicles, often grouped. Species numerous, difficult to distinguish.

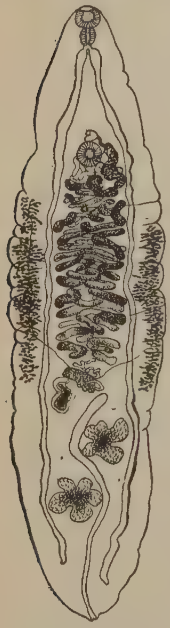

FIG. 357.—*Opisthorchis felineus.* ×12. Original figure drawn from M. Braun's material.

Opisthorchis felineus (Rivolta 1885)

Synonyms.—*D. felineum* Rivolta 1885; *D. sibiricum* Winogradoff 1892.

The living worm is yellowish-red, very transparent; with very mobile anterior end. The length is from 8 to 10 mm.; the breadth from 1.5 to 2 mm. The suckers are separated by about one-fifth to one-sixth of the body-length, and are about equal, 0.25 mm. in diameter. The anterior testis is four-lobed, the posterior five-lobed. The transverse ovary is very faintly lobed. There is a large, pear-shaped receptaculum. The vitellaria extend from behind the acetabulum to the ovary, in seven or eight groups of follicles on each side. The oval eggs have the cap clearly set off, and measure 30 by 11μ (Fig. 357).

First discovered by Winogradoff in Tomsk (Siberia), this parasite was later found in Russia, East Prussia, Roumania, Italy, France, Holland, Scandinavia, and possibly in Japan. The well-studied cases in the medical clinic at Königsberg i. Pr. numbered 40 between 1899 and 1909. In 25 of these cases the presence of the parasite was positively determined, but no symptoms were detected of liver or pancreas disturbance. In 10 cases enlargement of the liver and symptoms of disturbance in the abdominal organs were observed; and carcinoma of the liver, gall-duct, or gall-bladder occurred in five cases.

The life cycle of the parasite is not known, but Rindfleisch by a series of experiments on cats and dogs demonstrated that the last intermediate host is a fish (*Idus melanotus, Leuciscus rutilus, Tinca tinca*). The parasites survive several days after the death of the host and become mature in 12 days after ingestion by a dog or cat (Ciurea). Infection is thus evidently due to eating poorly cooked fish. This view is substantiated by the observation that among 40 patients infected with *Opisthorchis felineus*, nearly all carried at the same time *Diphyllobothrium latum* which is acquired by eating raw fish.

Opisthorchis viverrini and *O. noverca* are said to be abundant in man in Siam and India; they doubtless occur in children in those regions with effects similar to *O. felineus* and to Clonorchis. The species of Opisthorchis are much alike and very difficult to differentiate from each other.

GENUS CLONORCHIS Looss 1907

Much like Opisthorchis, differentiated by dendritic testes; branches laterad beyond intestinal crura on ventral side. Excretory bladder dorsal to testes, not curved between them, yet in form of an *S*.

The similarity of the eggs to those of Heterophyes and Metagonimus is pointed out by Leiper and will no doubt necessitate revising radically the data usually given on the incidence of Clonorchis.

Clonorchis sinensis (Cobbold 1875)

Synonyms.—*Distomum sinense* Cobbold 1875; *D. spathulatum* Leuckart 1876; *D. hepatitis innocuum* Baelz 1883; *Opisthorchis sinensis* R. Blanchard 1895.

Superficially this is much like *Opisthorchis felineus*. The length is from 13 to 19 mm., the breadth from two to four mm. The oral sucker measures from 0.58 to 0.62 mm., the ventral from 0.45 to 0.49 mm. Yellow-brown pigment granules appear in the parenchyma. The branches of the testes are very long; in anterior testis four branches, in posterior five. The ovary has one small and three large lobes. The vitellaria are fine, with follicles irregularly grouped, but broken and asymmetric. The eggs are from 26 to 30μ long, from 15 to 17μ broad (Fig. 358).

Clonorchis endemicus (Baelz 1883)

Synonyms.—*Distomum hepatis endemicum* Baelz 1883; *Distomum hepatis perniciosum* Baelz 1883; *Distomum japonicum* R. Blanchard 1886.

This is much like the preceding species. The length is from 6 to 13 mm., the breadth from 1.8 to 2.6 mm. The oral sucker is from 0.37 to 0.5 mm. in diameter; the ventral is usually slightly smaller. There is no pigment in the parenchyma. The vitellaria are continuous, not broken. The eggs measure 26 by 13 to 16μ.

Baelz originally recognized two forms and Looss differentiated a large *C. sinensis* common in China from a smaller *C. endemicus* abundant in Japan. More recent studies by Kobayashi indicate that these are in reality only a single species. They occur in the same hosts (man, dog, cat, and pig) and neither the effects nor the life cycles differ.

The parasites inhabit ordinarily the bileducts; they are found rarely in the pancreas and more often in the duodenum. Probably in the alimentary canal the worm is in the course of deserting the body of the host.

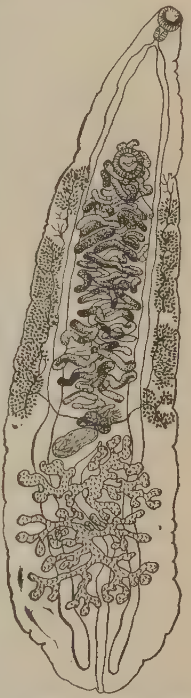

Fig. 358.—*Clonorchis sinensis*. Toto, original figure drawn from material from M. J. White, California. ×6.

Kobayashi has shown that in districts of Japan where the disease is prevalent the natives are infected by eating raw fresh-water cyprinoids; *i.e.*, the last intermediate host is a fish. In 12 species of native fish he found young encysted distomes with which experimental animals were infected and from which the adult worm developed in seven days; egg production begins in from 12 to 15 days and the parasite matures in from 23 to 26 days. In 1918 Muto showed that *Bythinia striatula* var. *japonica* is the first intermediate host.

Incidence.—Distributed over entire eastern and southeastern Asia, this parasite is especially abundant in South China, Tonkin, and Annam. In extreme cases infection runs as high as 40 per cent. in individual groups, though 16 to 20 per cent. is a more likely average for the entire population in badly infected regions. According to Asaoka among 411 school children in one village, 48 or 11.6 per cent. were infected by *Clonorchis sinensis*. Both first and second intermediate hosts of this parasite as well as cercariæ and encysted larvæ were observed.

In Annam, Mathis and Leger obtained records of 1250 natives among whom 349 were infected with Clonorchis, i.e., 4.5 per cent. of the children examined, 24 per cent. of persons from 15 to 30 years old, 36 per cent. of those between 31 and 50, and 48 per cent. more than 50 years old; in all, 32 per cent. of the men and 22 per cent. of the women carried the parasite. The increase in degree of infestation with age, which is strongly marked in their series, is attributed to multiplied infection and long life on the part of the parasite. Heanley found in Hong Kong 109 cases in 3300 necropsies and confirms the view that the degree of infection rises with the age of the host.

Infected Orientals have been reported in Panama, Central America, and the United States. All were adults and acquired the infection elsewhere. While some writers have expressed the fear that the parasite might become established on the North American continent, the life history indicates that infection of man here is obviously remote.

Symptoms.—The inception of the infection is not accompanied by any special symptoms. Enlargement of the liver takes place slowly and may proceed very gradually for a long time. In more severe cases, and especially among children, one encounters bloody diarrhea, accompanied by anemia, loss of weight, ascites and cachexia, with eventual death of the patient. In one recorded case no less than 21,000 worms were found in a single host.

Pseudamphistomum truncatum, a related parasite of the cat and dog in eastern Europe, has been reported from man in Russia. The life history is unknown but probably connected with some fish and infection is due to eating uncooked fish.

FAMILY SCHISTOSOMATIDÆ Looss 1899

Elongate digenetic distomes with weak suckers and greatly elongated body. No pharynx; crura unite to form median stem in posterior region. Sexes separate. Sexual organs simple. Male broader, with lateral margins rolled ventrad. Female cylindrical. Vitellaria median, close to median intestinal stem. Ovary elongate, anterior to union of intestinal crura. Eggs very large, thin-shelled, few in number.

GENUS SCHISTOSOMA Weinland 1858

Synonyms.—*Gynaecophorus* Diesing 1858; *Bilharzia* Cobbold 1859; *Thecosoma* Moquin-Tandon 1860.

Female filiform; male flattened, with margins rolled ventrad forming nearly closed groove, canalis gynecophorus, in which female is enfolded. Esophagus with many unicellular glands massed near posterior end; crura unite to form single median stem in posterior region. Genital pore median, post-acetabular in both sexes. Male with 3 to 6 simple testes, without cirrus sac. Female with single ovary, short simple uterus, and highly developed vitellaria. Laurer's canal wanting. Eggs oval, without cap when laid, containing ciliated miracidium with large gland cells opening at anterior tip. Parasitic in blood-vessels of mammals.

Schistosoma haematobium (Bilharz 1852)

Synonyms.—*Distomum haematobium* Bilharz 1852; *Gynaecophorus haematobius* Diesing 1858; *Bilharzia haematobia* Cobbold 1859; *Thecosoma haematobium* Moquin-Tandon 1869; *Distoma capense* Harley 1864.

The male is whitish, from 10 to 14 mm. long, 1 mm. broad, and from 0.14 to 0.17 mm. thick. The oral sucker is funnel shaped, with an overhanging dorsal lip; the acetabulum is slightly larger and stalked. The dorsal surface near the posterior end has spiny warts. Fine spines occur in the suckers, and also on the ventral surface in the canalis gynecophorus. There are four or five testes with large sperm vesicle and simple duct. The intestinal crura unite behind the testes to a median stem, although for short stretches they are again separated.

The female is 20 mm. long, only 0.28 mm. broad, and from 0.21 to 0.25 mm. thick. The oral sucker is slightly larger than the ventral. The intestinal crura unite behind the ovary to a single stem which extends zigzag to the posterior end. The genital glands are simple. The vitellaria, unpaired, extend from behind the ovary to the posterior end; with a median duct and lateral acini. The eggs are swollen, spindle-shaped, with a rudimentary filament on the posterior end, and measure from 120 to 190μ long by 50 to 73μ broad (Fig. 359).

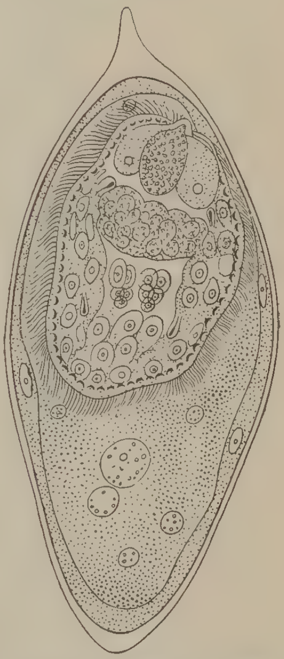

Fig. 359.—Egg of *Schistosoma haematobium*, from urine of man, enclosed miracidium full grown and ready to emerge. Magnified. (After Looss.)

Distribution.—This parasite, long known as the Egyptian blood fluke, inhabits the portal vein, the veins of the mesentery and of the viscera, especially the urinary bladder. By its presence the parasite gives rise to a disease known as schistosomiasis or bilharziosis, common since ancient times in Egypt, and along the east coast of Africa, including Madagascar. It occurs also in the interior, though much less frequently, and in Syria and Mesopotamia. Isolated cases are on record from Cyprus, Australia, and North and South America. Those in the Americas are probably introduced and there especially are confused with another species, *Sch. mansoni.* Eggs when deposited contain a fully developed miracidium, but this does not burst the shell until the egg comes in contact with water. While it was long believed that this parasite was introduced directly into the human host, Leiper in 1917 traced out the life cycle in a snail. The intermediate host is a species of Bullinus in Egypt, *Physopsis africana* and *Limnaea natalensis* in South Africa, and *Planorbis metidjensis* in Portgugal. The cercaria ultimately coming from the snail has been found free in the water, from which on the first occasion it assails the human host, making its way in through the skin.

Disease Acquired by Bathing.—Thus in a sense has been established the view, long maintained by English physicians in Africa, that the disease is acquired by bathing; for only in that way could they explain the great rarity of the complaint among the women when men and children in the same household were heavily infected. On the desert oases in Egypt and elsewhere, children bathe in the slow-flowing canal waters and in stagnant pools. Here abound those snails (*Bullinus brocchi, Physopsis africana*) that serve as intermediate hosts for the blood fluke and as a result free-swimming larvæ are present. That the infection takes place through the skin is indicated by the development of dermal areas of irritation, which the children scratch vigorously. Little girls are often infected, though older girls and women are relatively free from the disease. Here the infection is due to the use of contaminated water in washing infants. In country places women are often heavily infected when they do the washing. Children born and bred in Cairo are infected by bathing in unfiltered water drawn directly from the Nile, and some 10,000 are thus infected annually. From the poorest quarters, families go into the country at Easter, when the children paddle and bathe in the water. This single exposure is enough to produce an attack of the disease.

Incidence of Schistosomiasis.—Hematuria among children, especially boys, is reported by numerous observers (Nicolle, Cawston, *et al.*) from localities infested with *Schistosoma haematobium*, such as Egypt, Natal, Tunis, and doubtless is coincident with the distribution of the parasite. The disease attacks every race, sex and age (except the suckling) but is most frequent among those who are wont to bathe in open waters. Among the women and school girls in Cairo of the lower middle class, protected from contact with the Nile water, 27 per cent. were infected.* In one school, children of somewhat higher class showed also an average infection of 27 per cent. Among women of the lower middle classes from all parts of Egypt, examined at Cairo hospitals, the parasite was found only in 3 per cent. This suggests that an infection acquired in early life tends to disappear, and that probably repeated infections are responsible for the severe disease manifested in adult males in Egypt. The age incidence of schistosomiasis is practically identical throughout the world and, according to F. Milton,† this is explicable only on the assumption of acquired immunity.

Olpp‡ has recorded a most interesting case of a girl, infected at the age of 10 years when in Natal, who first displayed severe symptoms of the disease in Europe some 13 years later. The complex and serious disturbances characteristic of adult cases in infected regions may well be sequelæ of infections acquired in childhood.

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* Elgood, B. S., Bilharziasis among women and girls in Egypt. Brit. M. J., ii (Oct. 31, 1908), p. 1355.

† Milton, Frank, Bilharziasis, its incidence and eradication. Lancet, cxcviii (Jan. 24 1920), p. 196.

‡ Olpp, Ueber Maltafieber, Sprue, Bilharziosis und Bilharziasis mit Krankenvorstellungen, cxv (Dec. 10, 1918), p. 1417.

Symptoms.—Looss was able to distinguish two forms of the disease: (*a*) a mild type manifested by hematuria only and seen chiefly among school boys, and (*b*) a severe type complicated by cystitis, pyelitis, fistula, calculus, dysentery, and tumors; this form occurs among men only and almost exclusively among farm laborers. Among women the conditions, though often serious, rarely became so extreme. Looss reported that 30 per cent. of the native boys in a Cairo school, and from 80 to 90 per cent. of those from the outlying districts, suffered from the mild type.

Lithiasis is very common in Egypt and by many is regarded as due to schistosomiasis. In one case* a stone removed from the urethra of a 10 year old boy contained a nucleus of eggs of the blood fluke. In India, where the disease is rarer and confined to restricted localities, Hooton† reports the case of a girl five years old with intermittent hematuria, who suffered from an attack of fever thought to be malaria but later diagnosed as schistosomiasis.

Infection with the blood fluke is a cause of backwardness in children and routine examination of urine for ova is advised whenever boys in endemic areas fall behind in school work.

Treatment.—*Prophylactic.*—Since infection comes chiefly by bathing, the protection of drinking water against contamination is not an adequate safeguard against schistosomiasis. All personal contact with surface waters is dangerous as the infective agents, the cercariae, congregate near the surface. Storage of water for 36 hours suffices to kill all cercariae and subsequent contamination does not make the water dangerous unless it contains infected snails, or susceptible snails are present and sufficient time elapses to allow of the development of infective stages in them. Sand filters are not adequate for Leiper found that cercariae passed through four inches of desert sand within 15 minutes after the start of the experiment. Addition of copper sulphate to the water, in dilution of 1:1,000,000, judging from Chandler's‡ experiments, is apparently a simple and safe means of killing the snails in 24 hours. Water to be used for washing can be rendered non-infective by the addition of 1 part of cresol to 10,000 parts of water.

Medicinal.—Excellent results have recently been reported from the use of antimony in Bilharzia disease. According to Christopherson,§

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* Pfister, E., Urolithiasis und Bilharziasis, Arch. f. Schiffs u. Tropen-Hyg., xvii (Nov. 8, 1913), p. 309.

† Hooton, A., A case of bilharzia disease. Indian M. Gaz., xlix (May, 1914), p. 188.

‡ Chandler, A. C., Control of fluke diseases by destruction of the intermediate host. J. Agric. Research, xx (Nov. 1, 1920), p. 193.

§ Christopherson, J. B., Treatment of Bilharzia disease. Lancet, ccvi (May 24, 1924), p. 1071.

sodium antimony tartrate is the drug of choice. The sodium salt is less toxic, more soluble and quite as efficient as the potassium salt. They must be given intravenously, as oral administration is not effective and in subcutaneous tissues the drugs produce necrosis. Antimony in therapeutic doses has two actions: First and most powerful—it sterilizes the ova which spread the disease; second and later—it kills the parasite.

Technique.—Since the treatment is new and not without danger, due caution should be observed. A 1 or 2 per cent. aqueous solution of sodium antimony tartrate is used; it must be freshly prepared every day. Intravenous injections are given between meals (i.e., 2½ hours after a light meal and two hours before the next) on alternate days or three times a week. The initial dose for a child of 10 years is ¼ gr., increased by ¼ gr. at each injection until 1 gr. has been reached. Treatment is continued until from 12 to 15 gr. have been given. After a period of rest, resistant cases of schistosomiasis may require another course of treatment.

Results.—The first visible result is hematuria. On the ninth day the ova in the urine, much reduced in quantity, become granular; gradually the live ova disappear.

Effects.—During the injection a local blush is noted and the face and neck may become temporarily flushed. Before completion of the injection, a painful dry cough usually occurs. Others incidental phenomena are a metallic taste, dryness of the mouth, a feeling of constriction in the throat, tightness of the chest, and later, colicky pain in the abdomen; also giddiness, headache, nausea and diarrhea. These are signals that the dose should be decreased, instead of increased, at the next injection.

"Shock" should be treated by 0.5 c.c. of 1:1000 epinephrin solution, injected intramuscularly, followed by the local application of heat.

Emetin.—Often among colored races, antimony is not tolerated. The best substitute known is emetin, given intravenously for six days, in daily doses of ¾ gr. for a child of 10 years. The treatment should be stopped immediately if diarrhea or other symptoms of intoxication appear.* Cawston† suggests that intramuscular administration of emetin avoids the sudden cardiac depression produced by intravenous injections. The efficiency of emetin in schistosomiasis is still doubtful. Christopherson states that the large doses necessary are followed by peripheral neuritis and cardiac weakness.

Surgery.—At times surgical intervention is necessary. However, this is occasioned by the involved lesions of adults and is not called for with children.

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* Tsykalas, New ways of treating Bilharzia disease in Egypt. Wiener klin. Wchnschr., xxxiv (Dec., 1, 1921), p. 579.

† Cawston, F. G., The treatment of fluke disease. J. Trop. Med. and Hyg., xxiv (Oct. 1, 1921), p. 254.

Schistosoma japonicum Katsurada 1904

Synonym.—*Schistosoma cattoi* Catto 1905.

The male is 16 mm. long. It has no spinous warts. Both suckers have deep funnels, unlike in size; the oral 0.29, the ventral 0.34 mm. in diameter. Union of the crura takes place in the posterior third of body. The testes are elongate dorso-ventrally, in two compact rows of from five to eight lobules.

The female is 22 mm. long; very attenuate in the anterior two-thirds; heavier in the posterior third. The oral sucker measures 64μ, the ventral from 52 to 72μ in diameter. The eggs are oval without spines (sometimes with a minute vestigial process), from 75 to 90μ long, and from 50 to 75μ broad (Figs. 360, 361).

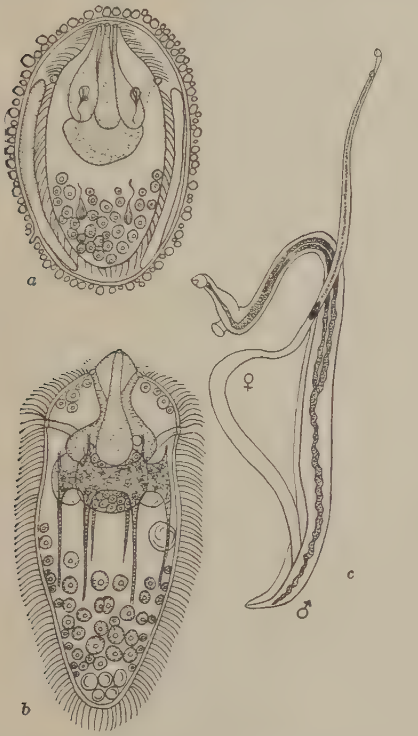

FIG. 360.—*Schistosoma japonicum.* *a,* miracidium in eggshell. ×420; *b,* free swimming miracidium. ×420; *c,* mature worms in copula. ×8. (After Faust and Meleny.)

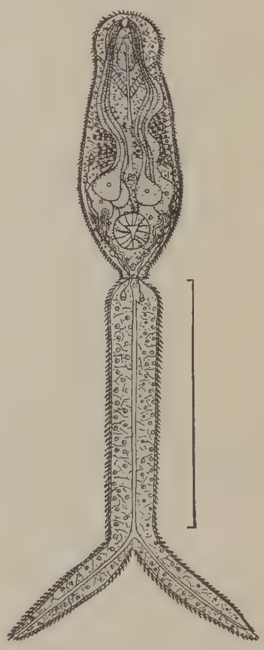

FIG. 361.—Free swimming cercaria (infective stage) of *Schistosoma japonicum.* ×325. (After Faust and Meleney.)

The intermediate host, according to the work of Miyairi and Suzuki 1913, is a small snail of ricefield ditches and swamps. Although originally called Blanfordia, it is correctly named *Katayama nosophora* Robson. The snail is infected in any given region about proportionally to the incidence of the disease. The cercaria is photophobic and shows very little resistance to drying or high temperature. Aside from man, it is said that cattle, horses, goats, pigs, dogs, cats, mice, rats, monkeys and guinea pigs are easily infected. A coating of oil renders the skin impervious. Ordinarily the worms penetrate the healthy skin through the hair or root sheath. At the site of the invasion slight though definite changes can be recognized microscopically. The penetration of the skin causes an itching which is followed by Kabure, a skin disease. In China it is known as Yangtse, Hankow, urticarial or river fever, the etiology of which was first determined by Houghton.

Distribution.—This parasite was not discovered until 1904, when Katsurada found, in so-called Katayama disease, ova which he recognized as those of Schistosoma. Catto found the same species at the necropsy of a Chinese at Singapore, and Woolley reported its occurrence in the Philippine Islands. The species is common in various provinces of central and southwestern Japan. In China it occurs abundantly in the basin of the Yangtse river, and from there the first case of ova in fever was reported by Logan in 1908.

The disease is distinctly a country malady and is especially prevalent among men. The infection is acquired by bathing or, specifically, by immersing the extremities in water. This was demonstrated on experimental animals, and later by a Japanese investigator (Matsura) who immersed his own extremities in naturally infected water. A relatively short time (1½ hours or less) is required for the cercaria to enter the skin, and the period of development to the egg-laying adult is about four weeks. The invasion is accomplished by the free swimming cercariæ which are released into the water from the snails that function as intermediate host.

Life History.—Faust recently* in summarizing his researches on the life history of the parasite, outlined the contrast between this and the preceding species: (1) The free swimming infective miracidium of *Sch. japonicum* moves in the top stratum of the water and only mollusks found there are exposed to infection. (2) Free-swimming infective miracidia of *Sch. haematobium* are equally distributed through the water and all snails in the vicinity are exposed to infection. (3) Only operculate snails in the genera Katayama and Onchomelania harbor *Sch. japonicum* infection; several closely related species are involved. (4) Nonoperculate snails of the genera Isodora and Planorbis harbor larvæ of *Sch. haematobium;* here also related species are involved.

The cercaria attacks the skin by proteolytic ferments exuded from the cephalic ducts, and thus penetrates into the human host. In the latter it uses blood channels for migration, passing normally through the capillaries of the lung to the systemic circulation. Only those that pass through the mesenteric capillaries into the mesenteric veins are apparently able to continue growth. The sexes were observed in copula as early as the seventeenth day after infection, and ova appeared in the feces on the twenty-eighth day.

Age Incidence.—As in the case of the previous species, the human host is infected in proportion to exposure to infected waters, most of all, laborers in the ricefields, and least of all, women confined to the house by domestic and social duties. Newcomers are taken sick after the first work in ricefields, but repeated infections are not frequent, even under exposure. Among children it is noted that boys who bathe in streams or work in the fields are the only ones who ordinarily acquire the disease, and are more affected than adults. Yet cases among children are often mild and unrecognized, and one should not underrate these conditions, as the disease is persistent and its effects are cumulative in later life (Fig. 362). Eggs of this parasite were found in the feces of 3 out of 22 newborn infants in an endemic area. In the province of Okayama (Japan), from 56 to 67 per cent. of those subjected to fecal examination were infected. In Tonkin and Annam 32 per cent. of the males examined were infected, 24 per cent. of the females, and only 4 per cent. of the children.

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* Faust, E. C., Reactions of miracidia of *Schistosoma japonicum* and *S. haematobium* in presence of their intermediate hosts. J. Parasitology, x (June, 1924), pp. 199-204.

Katayama Disease.—The parasite gives rise to a protracted and at times fatal malady, known in Japan as the Katayama disease. Enlargement of liver and spleen is general and is accompanied in the Yangtse valley, at least, by a recurrent fever with a temperature of 102°F. (40°C.) at evening and a fall to normal by morning. Accumulations of eggs in the liver produce granulomata, the parasitic embolic cirrhosis of Yamagiwa. In the colon they produce polypoid growths, often extensive and branched; bloody mucous diarrhea ensues, and general anemia (Fig. 362).

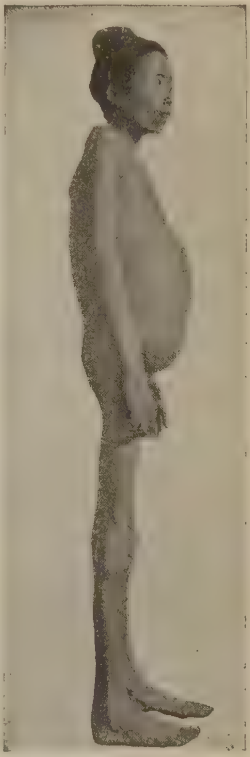

FIG. 362.—*Schistosoma japonicum*. A late case of schistosomiasis, aged 21, showing intense emaciation and ascites. The photo was taken after 3800 cc. of fluid had been removed from the abdominal cavity. Note tendency to constriction in the midabdomen. (After Faust and Meleney.)

Treatment.—The problem is of great magnitude in the rice growing regions of China. Extermination of the snail intermediate host is hopeless according to Faust and Meleney* who recommend control of feces disposal, avoidance of wading in waters in infected areas, protection of skin by workers in rice fields, and extensive specific treatment of the disease.

Emetine and preparations of antimony have been found to have specific lethal action but emetine has not been sufficiently used in schistosomiasis japonica to warrant sweeping claims. Tartar emetic treatment, properly carried out, effects a cure in 50 per cent. of cases of this disease; nearly 30 per cent. more are much improved, most of the remainder have applied for treatment too late.

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* Faust, E. C. and Meleney, H. E., Studies on Schistosomiasis Japonica. Amer. J. Hygiene, Monogr. Ser., No. 3, Mar. 1924.

Schistosoma mansoni Sambon 1907

Very similar to *Sch. haematobium;* from experimentally infected mice Leiper bred worms with the following characters: Males with eight or nine testes and very long terminal alimentary cecum; females with an ovary in the anterior half of the body, short uterus with but one egg, and extensive vitellaria occupying the posterior two-thirds of the body. The ova are from 124 to 170μ long and from 56 to 89μ wide, with a lateral spine from 17 to 26μ long and 5 to 9μ wide.

In Egypt the intermediate host is *Planorbis boissyi* and the unknown life history is probably similar to that of *Sch. haematobium.* Leiper was able to differentiate the cercariæ by size of suckers, length of tail, and other minute details.

In 1903 Manson conjectured that cases from the West Indies represented a form different from the Egyptian *Sch. haematobium* by virtue of the presence of a lateral, and not a terminal spine on the eggs, and by reason of clinical conditions. The eggs were voided with feces rather than urine, and pathologic modifications involved the rectum instead of the urinary passages. It appeared later that this was the only form found in the Congo and some other parts of Africa, as well as in the West Indies, into which its introduction seems to have been the result of the slave trade. The existence of a separate species is now established, but in distribution and clinical significance it is not yet well differentiated from the older Egyptian form with which it is associated in a mixed infection in certain regions, as is reported for Natal (Cawston).

Incidence in Children.—This species is known to occur in the Congo, Brazil, West Indies, Panama, and Venzuela, as well as in some places in Egypt. In Porto Rico, the disease is found in country patients, and especially in children who have bathed in a small tributary of the River Vivi in Utuado. Gonzales has investigated the species carefully. It is prevalent only in low-lying regions, particularly swampy grounds on which cane is cultivated. The disease is not common and is benign in form, with spontaneous cure on removal of the patient from the infected center. Two cases, without the usual symptoms of schistosome infection, are known from Santos, Brazil. Both were in children aged seven and eight years respectively, and ova of *S. mansoni* were found in the stools. The intermediate host was a Planorbis, probably *P. centrimetralis.* The first patient was treated with emetine and the ova disappeared. In Gonzales' record in Porto Rico, among 356 cases there were 32 under 10 years of age and 127 between 10 and 19. In Venezuela cases are recorded from boys, and eggs and blood appeared in the stools of an infant only five years old, recently brought from Martinique. In French Guinea, intestinal infection among children, chiefly in boys from 5 to 15 years, varied from 10 to 60 per cent. in different localities (Clapier).

Schistosoma bovis, common in cattle in India, has been reported from a native boy, 8 years old, in South Africa. More precise study may show that this species is often confused with the others hitherto recorded from man.

FAMILY PARAMPHISTOMIDÆ Fischoeder 1901

Among the many species, two, viz. *Gastrodiscoides hominis* and *Watsonius watsoni* have been reported from man in India and West Africa where they appear despite scanty records to be important human parasites.

II. CESTODA

Introduction.—The tapeworms are elongated, ribbon-like, or rarely cylindrical flatworms (Plathelminthes) which, in all save exceptional instances, are recognizable by the division of the body into joints or segments. They are also differentiated from the flukes, to which they are somewhat closely related, by the fact that no alimentary system has been detected at any stage. Nutrition is obtained by the absorption of already digested food from the cavities of the host. A tapeworm infection is usually recognized by the joints or segments which are set free periodically from the body of the worm, and are discharged from the host with the feces. Such individual segments frequently have marked power of locomotion and by virtue of their extended movements are often diagnosed as independent animals. An examination with a low power lens is sufficient to show the absence of the diverse organ systems that characterize the complete animal; the segment is little more than the extended uterus crowded full of eggs. Other organs have been resorbed in the process of accumulation of the ova, so that the segment is ultimately reduced to an egg sac or protecting cover in which the eggs are held, and by which they are protected until proper conditions for development are furnished.

Adult Anatomy.—At the smaller end of the body is the head or scolex, a bulbous swelling which carries organs of attachment, the suckers and hooks. Hemispherical cup-shaped suckers, or acetabula, occur in the taenioid worms; elongate slit-like grooves or bothria are found in bothriocephalid types. A circle of large hooks surrounds a muscular cushion, the rostellum, at the apex of the head in most tæniæ and large numbers of minute hooklets are present in some other forms. A constricted region just behind the scolex is designated the neck; it may be wanting, but usually is delicate and hence the breaking point when the body is under strain. By virtue of its small size the head is often overlooked or it may remain in the host. The region behind the neck is faintly divided by cross furrows into segments or proglottids, which become more distinct toward the end of the chain.

Proglottids.—In both younger and older proglottids one can see on either side near the margin a dark strand which is the longitudinal nerve trunk, and a broader, lighter band, the lateral excretory canal. The latter is joined by a transverse canal to the lateral canal on the opposite side, and possesses a network of finer tubules in the tissue, which is only rarely visible in part. There are, in fact, two such longitudinal canals on each side, but one is ordinarily much larger and more conspicuous than the other. The lateral nerve trunks are joined by a ring commissure in each proglottid, and connect with a network of smaller fibers. But such details can be demonstrated only by special technique. Layers of muscle fibers occur in the external or cortical region of the proglottid and are often thick enough to obscure seriously the location of deeper-lying organs. The relative position of these structures can be readily understood from the cross-section of a proglottid. Each proglottid (Fig. 363) contains a single or double set of reproductive organs which are gradually differentiated from the neck to the end of the chain. The precise structure of these organs is utilized as a basis for distinguishing various groups of tapeworms. Proglottids at the height of reproductive activity have organs of both sexes.

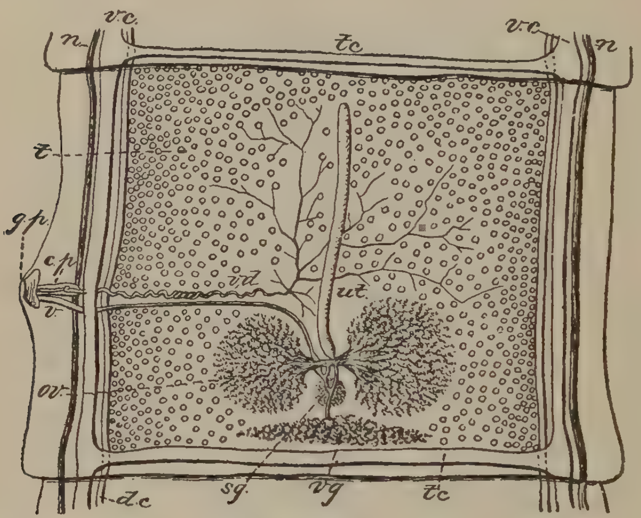

Fig. 363.—*Taenia saginata;* sexually mature proglottid; *cp*, cirrus and pouch; *dc*, dorsal canal; *gp*, genital pore; *n*, nerve; *ov*, ovary; *sg*, Mehlis' gland; *t*, testes; *tc*, transverse canal; *ut*, simple uterus; *v*, vagina; *vc*, ventral canal; *vd*, vas deferens; *vg*, yolk gland. Magnified. (Modified from Leuckart.)

Male Organs.—The male system is relatively simple. From the testes, which may be scattered follicular structures or condensed masses limited in number, the sperm cells are conveyed by a set of collecting tubules (vasa deferentia) to a reservoir (vesicula seminalis) which is usually adjacent to or included within the sheath of an intromittent organ known as the cirrus. This communicates with the exterior by means of a genital cloaca and the common genital pore, which may be lateral as in Taenia or superficial as in the bothriocephalid cestodes. Since the genital cloaca includes the vaginal orifice, self-fertilization is possible and has been observed in numerous instances. As the proglottid advances in age the testes gradually disappear, until in proglottids near the end of the chain, the main vas deferens, the collapsed vesicle and the reduced cirrus are the only recognizable parts of the male system.

Female Organs.—In the female system the ovary usually is a median, bilobed or paired organ of variable form and conspicuous in size. With it are connected accessory glands, known as vitellaria or yolk glands, and Mehlis' gland or the shell gland, the function of which is probably incorrectly indicated by the name in common use. The vagina, which runs from the genital cloaca to the glandular complex just described, bears usually an expansion known as the receptaculum seminis. A large tube designated the uterus joins the complex in or near Mehlis' gland. At first the uterus is simple and empty but, as it becomes filled with developing eggs, lateral branches form and it comes to occupy in older proglottids nearly the entire space within the body wall. This gives to discharged segments their characteristic appearance. In the taenoid worms the uterus has no external orifice and the eggs accumulate in masses, almost filling the proglottid; but in bothriocephalid types there is a uterine pore through which the eggs are gradually extruded. In both cases the embryo has developed considerably before the egg reaches the external world.

The Embryo.—The completed embryo of the tapeworm, known as the oncosphere, is a small spherical mass bearing six hooks. In the bothriocephalids, the oncosphere is enveloped in a ciliated membrane in which it leads a brief free swimming existence after hatching (Fig 364). In the taenoid cestodes, it remains in the egg shell protected by characteristic membranes until it reaches a new host, thus it possesses no free-living stage and is transferred passively to the new host.

Once having arrived in the alimentary canal of a suitable host, the hexacanth embryo bores its way out and, encysted in the connective tissue or at some other point in the body, develops into the bladder-worm, a spherical larva (cysticercus) in Taenia, or to a spindle-shaped plerocercus in some other forms. In the cysticercus a knob-like ingrowth from the outer wall of the sphere becomes gradually the head of the tapeworm in reverse, and with the completion of the process the larva reaches the stage in which it is ready to infect a new host. The transfer is passive and usually accompanies the consumption by a suitable host of the flesh containing the fully differentiated bladder-worm. When by digestion the cysticercus is released from enveloping tissue, the inturned head is forced out and, attaching itself to the wall of the host intestine, begins its growth. At the beginning of this process the bladder is lost by digestion. From the head the slender neck elongates and later is divided into proglottids. These gradually develop reproductive activity and ultimately, by the accumulation of ova, become ripe for discharge from the adult host.

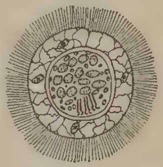

Fig. 364.—Free swimming embryo of *Diphyllobothrium latum.* Magnified. (After Schauinsland.)

Historical.—From their large size, both tapeworms and bladder-worms are conspicuous human parasites and must have been recognized even by prehistoric peoples. They are well described and their treatment discussed in the most ancient medical writings. The extensive sections on these forms in the famous Papyros Ebers (1500 B.C.) are taken from earlier, nonextant medical treatises. Hippocrates considered the "pumpkin-seed" fragments as diagnostic of tapeworm infection and discussed an operative measure for the removal of echinococcus bladders. Ancient views on spontaneous generation led Galen to speak of the tendency of the liver to "produce" bladder-worms in its fascia, and the origin of the tapeworm was attributed to an exudation of the alimentary canal, or to the thickening of surplus food such as milk or cheese. At a later period tapeworms were attributed to pathologic processes associated with various diseases, while bladder-worms were regarded as tumors. The genetic connection between the two was first demonstrated by Küchenmeister about 1850. The large human cestodes were not distinguished as separate species before 1600 A.D., and the smaller forms were entirely unknown until very recent times.

Species Rare in Children.—The large, well-known tapeworms of man are not unknown in children. Indeed rare cases of all three forms have been reported from suckling infants, but ordinarily no one of the three is likely to be parasitic in a child. Furthermore, while the beef tapeworm, *Taenia saginata*, is not uncommon on the North American continent, both the pork tapeworm, *Taenia solium*, and the fish tapeworm, *Diphyllobothrium latum*, are rare even in adults. Diagnosis is easy because the joints are large in size and hence not easily overlooked. But these three types are really parasites of the adult human host and of little significance in children.

Tapeworms Characteristic of Children.—Among the 30 or 40 types of tapeworm recorded from the human host, there are at least four which are very characteristic parasites of children, having been obtained rarely, if at all, from other hosts. These forms stand in conspicuous external contrast with the species mentioned in the previous section. They are diminutive in size and for that reason somewhat easily overlooked. At the same time, however, they may be present in considerable numbers in a single host, whereas the large tapeworms either occur singly or, in a very small number of specimens, in a single host. It is only in recent years that knowledge of the occurrence of these smaller species has been gained. Steadily growing information indicates that they are relatively frequent, and that one form occurs commonly among children. One of these species has not yet been recorded outside of the tropical zone, but of another a well-known parasitologist says that it is the most common of all human tapeworms. Because of the ease with which these smaller species may be overlooked, greater care in diagnosis is necessary on the part of the physician. By virtue of their small size, the range and frequency of these species is only imperfectly known. More emphasis should be placed on this situation. An examination of standard works on children's diseases reveals that in most cases these parasites are not even mentioned.

Diagnosis.—The material available for diagnosis is usually taken from stools and consists most frequently of fragments conspicuous by size and appearance. Whenever reasonable grounds exist for the tentative acceptance of the general and, usually erroneous, popular diagnosis of "worms" in infantile disorders, a careful microscopical examination should be made of fresh fecal discharges. Such examination may reveal unnoticed proglottids or ova of the smaller cestode species, and for each of these there are characteristic features of diagnostic value. Whenever possible the diagnosis should be confirmed by careful examination of the cestodes removed by administration of a vermifuge. Among the numerous pseudoparasites (*q.v.*) which threaten to mislead the diagnostician, one of the most deceptive here is the mucus cast from the intestine.

The following keys deal only with forms thus far reported for North America, and any diagnosis should be checked by careful comparison with the extended descriptions of other known species. When the material under scrutiny seems not to agree with the description given, most precise study is demanded before publication of the results if errors are to be avoided. The mistakes already permanently recorded in medical literature make it advisable also to consult some expert in the field in advance of publication.

KEY FOR DETERMINATION OF HUMAN CESTODES REPORTED FROM NORTH AMERICA

(*A*) Adult forms complete, with head or scolex in place.
  1. Head with four acetabula. Order Cyclophyllidea 3, 4.
  2. Head with two bothria. Order Bothriocephaloidea.
    Only one genus reported........................ Diphyllobothrium.
  3. Large forms; when fully grown from one to several meters long, with 500 to 1000 proglottids.....................................Taenia.
  4. Small forms; a few millimeters to half a meter long; chain slender........ Several genera....B2

(*B*) Proglottids single or in groups from stools; only fragment of worm at hand.
  1. Proglottids large, heavy, muscular.
    (*a*) Proglottid broad, noticeably thicker in center with uterus in form of rosette..................................*Diphyllobothrium latum.*
    (*b*) Proglottid long, not thicker at center; uterus with central stem and lateral branches.....................
      Taenia saginata (see page 980).
      Taenia solium (see page 984).
      Taenia confusa (see page 987).
  2. Proglottids small, delicate.
    (*a*) Genital pore on one margin only.
      Proglottid thin, much broader than long.......................
        Hymenolepis nana (see page 992).
        Hymenolepis diminuta (see page 997).
      Proglottid oval, thick...*Davainea madagascariensis* (see page 1003).
    (*b*) Genital pore on each lateral margin.
      Proglottid melon-seed shaped....*Dipylidium caninum* (see page 999).

The Ova.—Cestode ova in feces are not difficult to recognize and differentiate from those of other helminthes. The cestode egg is oval and provided with a thin outer shell within which are embryonic membranes of characteristic appearance. In the bothriocephalid egg, this takes the form of a ciliated mantle; in the taenioid it is a thick, spherical layer often radially striated, and formerly known as the second shell. The minute oncosphere which lies within these membranes may always be recognized by the three pairs of delicate hooks. The minute size of the oncosphere and the absence of structural features make it difficult to distinguish oncospheres of different species of cestodes.

Habitat of Adult Cestodes.—The alimentary canal, and particularly the small intestine, is the normal habitat of the adult cestode, in man. They desert the canal at the onset of many diseases and sometimes wander apparently without cause into the liver or the stomach, from which specimens have been vomited. The erratic occurrence of cestodes in the bladder and their emergence from the navel or from fistulæ or abscesses are explained by readily recognizable pathologic conditions. Such cases are very rare. Proglottids passed *per anum* often display marked independence of movement and live for some hours, during which they migrate far from the original place of deposit and may be found on the floor or wall of rooms or outhouses. This activity has often led to their diagnosis as flukes.

Symptoms.—The effects produced by tapeworms are subject to considerable variation with the species involved, also with the personal condition or sensitivity of the host. Rarely no symptoms at all are manifested. Indefinite pains, a sense of distention, and ravenous hunger are not unusual. Usually there are moderate disturbances, and in some cases extreme symptoms have been noted. These are not explicable on the basis of the loss of the nutriment abstracted by the parasite, although that is not inconsiderable and may well be a contributing factor. Anemia is a common manifestation and in the presence of certain cestodes assumes a pernicious character. Nervous and epileptic symptoms have been observed often, and, like the anemia disappear promptly with the removal of the tapeworms. These symptoms are ascribed to toxins produced by the cestodes and absorbed by the host. The fluid from a hydatid cyst has been shown by experiment to be toxic, and extracts have been prepared from various tapeworms that manifest extreme toxic effects. Such results are apparently obtainable only from old or dead worms, and it has been suggested that man is supersensitive to the accumulated metabolic products of the cestodes.

Treatment of Cestode Infection.—Aspidium, pomegranate, pumpkin-seed, cusso, kamala, thymol and chloroform have been used in the treatment of tapeworm; aspidium is perhaps the most generally useful remedy.

Technique.—Before the administration of an anthelmintic, several days should be devoted to preparation of the bowel.* The dosages here given are for a child aged 10 years. The child should take only a light diet and should gradually cleanse the bowel by the use of:

℞.	Magnesii sulphatis....................................	30
	Spiritus chloroformi	7
	Aquæ, q.s. ad..	100

M. Sig.: A tablespoonful in water, 3 times a day, an hour before meals.

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* Osborne, O. T., and Fishbein, Morris, Handbook of Therapy. Chicago, A.M.A. (1923), p. 295.

A soap-and-water enema and a final cleansing dose of 2 tablespoonfuls of the above mixture are given the night before the treatment. The next morning, after the bowels have moved, give

℞. Oleoresinæ aspidii .... 4 gm.
Fac capsulas VIII
Sig.: 1 capsule with one-half glass of hot water at 9 a.m., 9:15, 10:00, and at 10:15 a.m., making 4 capsules in all. (Important: Before taking the above capsules, each one should be uncapped.)

Instead of gelatin capsules for the male fern, a drink may be prepared with mist. amygdalæ comp. and flavored with oil of peppermint. Between 10 a.m. and 2 p.m., a physician or thoroughly trained nurse should remain with the child. At 12 m., three tablespoonfuls of the magnesium sulphate mixture are given to insure rapid passage of the male fern through the intestine, lest too much absorption take place. The child stays in bed all day. During the morning no nutrition should be taken other than bouillon or water. Any food desired may be given after 1 p.m.

The motions should be passed into a vessel containing warm water and strained through black muslin to facilitate search for the head.

Duodenal Tube Method.—Introduction of the anthelmintic directly into the duodenum, where the head of the tapeworm lodges, is favored for older children by Gantt and Wiest,* and by Schneider.† They hold that this method insures expulsion of the whole worm, without leaving the head behind; there is no nausea and vomiting, and the treatment does not have to be repeated.

ORDER CYCLOPHYLLIDEA Braun 1900

These are polyzoic cestodes with four powerful acetabula on the scolex and often also an apical rostellum with or without hooks The proglottids are distinctly marked off externally but do not separate until ripe. There is no uterine pore; the common sexual pore is marginal. The eggs are thin-shelled and without cover. The adult lives in the alimentary canal of higher vertebrates. The human parasites are all in one family, the Taeniidæ.

FAMILY TAENIIDAE Ludwig 1886

GENUS TAENIA Linnaeus 1758

Species large. Ripe proglottids much longer than broad. Genital pore irregularly alternating. Testes numerous, ovary double; uterus median longitudinal stem with lateral branches. Larva large with single scolex (Cysticercus), triple scolex (Coenurus), or multiple scolex (Echinococcus). Adults in man and in some carnivora; larvæ in man and in some herbivora. Some authors recognize separate genera on the basis of the character of the larva.

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* Gantt, W. H., and Wiest, P. F., Simple and effective method of administering anthelmintics. Therap. Gaz., xlvi (July, 1922), p. 471.

† Schneider, H., Duodenal tube in treatment of tenia infestation. Wien. klin. Wchnschr.. xxxvii (April 3, 1924), p. 338; abstr. J.A.M.A., lxxxii (May 17, 1924), p. 1659.

Taenia saginata Goeze 1782

Synonyms.—*T. inermis* Moquin-Tandon 1860, Laboulbène 1876; *T. dentata* Nicolai 1830; *T. lata* Pruner 1847; *T. mediocanellata* Küchenmeister 1855; *T. tropica* Moquin-Tandon 1860; *T. nigra* Laboulbène 1875; *T. africana* v. Linstow 1900; *T. tonkinensis* Railliet and Henry 1905; *T. philippina* Garrison 1907; *T. bremneri* Stephens 1908; *Taeniarhynchus** *saginatus* Weinland 1861.

The unarmed human tapeworm, often designated the beef tapeworm, averages from four to eight meters in length though much larger measurements are occasionally cited. The head is pyriform, four sided, and measures from 1.5 to 2 mm. in diameter; it has neither rostellum nor hooks, but a shallow depression at the apex which is often pigmented. The suckers are elliptical and about 0.8 mm. long. The neck is long and distinctly narrower than the head. The proglottids number more than 1000, often about 2000; the first are broader than long, a condition that obtains despite increase in size until near the end of the chain, when they assume the characteristic "pumpkin-seed" form; these terminal proglottids measure from 16 to 20 mm. in length and 4 to 7 mm. in breadth. The genital pore lies posterior to the center of the proglottid. The uterine branches are numerous (from 15 to 30), slender, and dichotomously branched. The eggshell is delicate, with one or two polar filaments, often missing; the embryophore is ovoid, measuring 30 to 40 by 20 to 30μ (Fig. 346). Ripe proglottids are detached singly; they are very active and mobile; they leave the intestines independently between stools (Fig. 365).

The adult lives exclusively in the small intestine of man, with the head attached to the wall near the pylorus. Despite the absence of hooks, it maintains its position strongly and is difficult to dislodge. Stieda has described a case in which the parasite had bored its way through the wall of the duodenum and into the pancreas. The absence of preformed orifices and abscesses, with other evidence, left little doubt that the migration was active. The parasite rarely occurs other than singly in its host; the first infection appears to produce a sort of temporary immunity, disappearing with the expulsion of the worm.

Proglottid.—The structure is best visible in a proglottid (Fig. 363) taken about 40 to 50 cm. from the head. Diagnostic for this species is the unequal size of the ovarian lobes, that on the pore side being smaller, and without any accessory lobe as in *T. solium*. In general the proglottids appear more open and the organs manifest greater anteroposterior extension than in *T. solium*. In ripe proglottids the uterus, easily seen after treatment with acetic acid, appears more crowded, the lateral branches are much more numerous, and two or three opposite the pore are stunted or lacking (Fig. 366*A*).

Larva.—The larva, known as *Cysticercus bovis*, occurs in the muscles and viscera of cattle. When the eggs by chance are brought into the stomach of cattle, the hexacanth embryos are set free by digestion. They bore into the intestinal wall and are thought to enter capillaries of the portal system or lymphatics. At this time they measure 20μ in diameter. They enter the general circulation and are widely disseminated. By preference they select the connective tissue in voluntary muscles and heart tissue. Being minute and widely scattered they are difficult to detect. In six weeks they have grown to a size of 3

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* This genus, established to include the unarmed taenias, does not seem justified in view of the close similarity of the species in all other structural details.

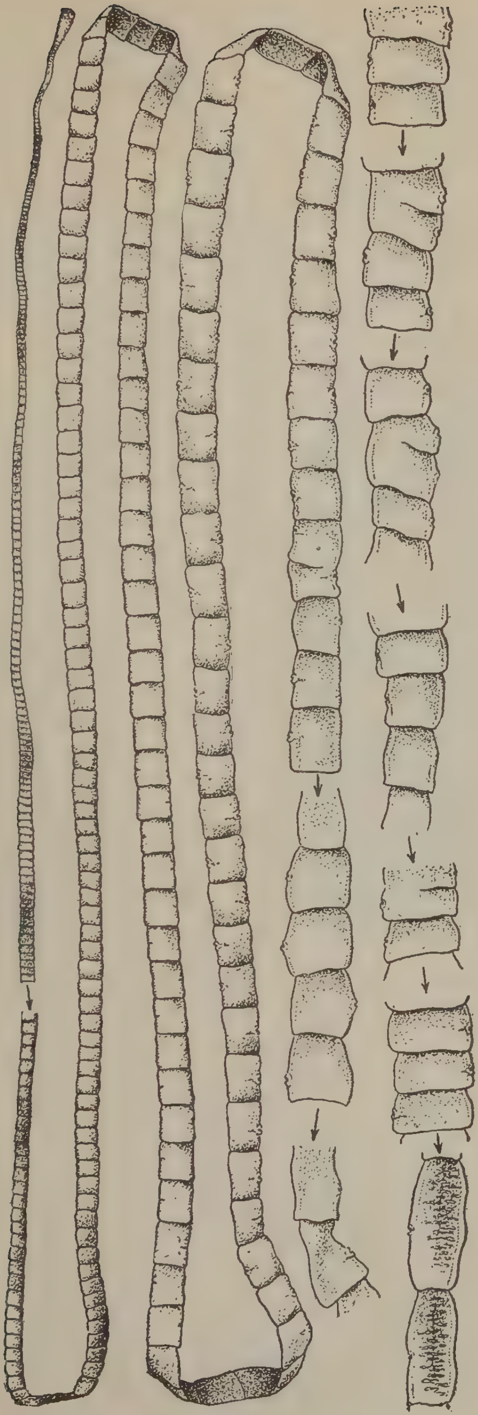

FIG. 365.—*Taenia saginata;* adult natural size. (After Stiles.)

by 5 mm. with an inverted scolex 1 mm. in diameter. In 24 weeks these measurements are 4, 6, and 2 mm. Their life span is short, since in less than eight months they are completely calcified. According to Perroncito, a temperature of from 45 to 46°C. is fatal, but the center of a roast ordinarily does not reach that level. Cold storage conditions destroy the life of all bladder-worms in a piece of beef within three weeks.

Variations.—In 1861 Leuckart fed ripe proglottids of this tapeworm to calves and obtained the then unknown Cysticercus. These results have been experimentally confirmed often since then. Man also has been experimentally infected with the adult tapeworm by eating flesh containing living *Cysticercus bovis.* The worm makes an average growth of 72 mm. or about 13 to 14 proglottids daily. *Taenia saginata* seems prone to variation and malformation. Excessive pigmentation was the cause of a type regarded as a separate species and named *T. nigra* by Laboulbène in 1875. The occasional disappearance of segmental boundaries produces a proglottid with two pores and two sets of reproductive organs. Welch has described such an unsegmented region 5 cm. long. Intercalated proglottids and irregularly triangular segments are common. By the falling out of the central portions in a series of proglottids a fenestrated chain is produced.

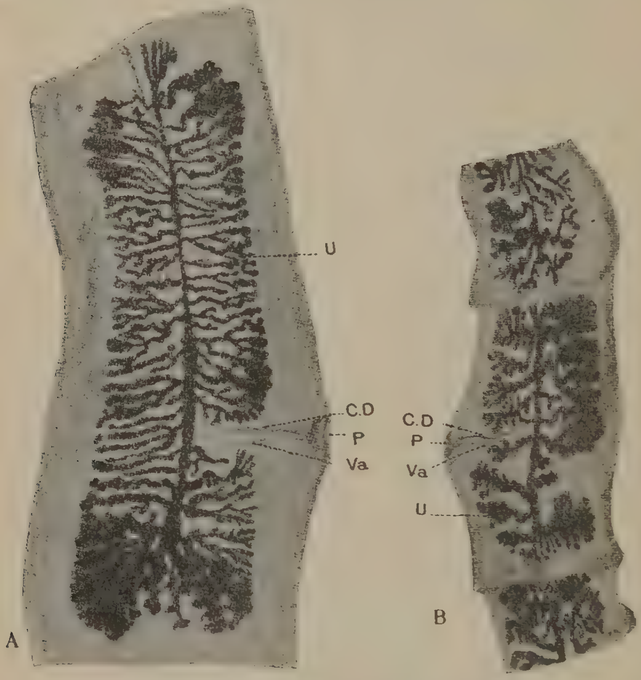

FIG. 366.—Ripe proglottid of (*A*) *Taenia saginata* and (*B*) *Taenia solium*, showing branching uterus (*U*) crowded with eggs and remnants of vas deferens (*CD*), genital pore (*P*), and vagina (*Va*). Magnified. (After Joyeux.)

This which as a separate species was named *T. fenestrata* is doubtless due to excessive accumulation of eggs in the uterus and undue pressure on or weakness of the lateral walls. A prismatic or triradial variety, Y-shaped in cross section, and having a scolex with six acetabula, was described a century ago and has been seen often since then. Oncospheres with extra hooks and bladder-worms with six suckers, or with only three, two, or one or even no suckers, are also among the malformations described. Such numerous and extreme variations make the positive determination of aberrant forms difficult and suggest caution in describing unusual types as new species. A malformation of the type of a meristic variation has been taken from an infant.

Distribution.—The beef tapeworm is cosmopolitan in distribution. It is, of course, most common among people who eat beef rare, and least common where beef is used well-cooked or not eaten at all. Its occurrence in young children may generally be traced to the practice of feeding scraps of rare beefsteak and to the contamination of the hands of the parent or the kitchen utensils. In Africa, Europe and America the parasite has been abundant and apparently on the increase during the last century. This tendency has in recent years been counteracted by the growth of the packing industry and cold storage methods. However, in 1913, the larvæ occurred in 0.6 per cent. of all beef carcasses slaughtered under federal inspection; in special localities it ran as high as 5 per cent.

Incidence in Children.—Cases in children occur at all ages though they are not common. Schloss records five cases among 280 children in New York; Bass and Gage three cases in 577 examined in New Orleans, and H. B. Wood ten in 62,785 examinations in state laboratories of the South during 1911 and the first quarter of 1912. *Taenia saginata* has been reported for a six-month old child fed on milk alone. Ransom has suggested several ways of explaining the occurrence, which was doubtless due to the transfer of a cyst directly or indirectly to the milk by some instrument, such as a knife, used in cutting infested meat. Several cases of the bladder-worm in adults in Europe are on record. Watkins-Pitchford maintains that *C. bovis* is not rare in man since three cases have recently come to the notice of the South African Institute for Medical research in Johannesburg. Since *C. cellulosæ* may lack its hooks, even careful workers may diagnose a hookless bladder-worm of this species as *C. bovis*.

Prophylaxis.—The destruction of the bladder-worm by cold storage is a valuable aid to sanitation. Ransom found that exposure for six days to a temperature of from 11 to 15°F. left no living *Cysticerci bovis*, though in control pieces of the same meat left unfrozen all were active after eight days. In "coolers" at the temperature ordinarily used, 21 days were necessary for the destruction of life in all of the bladder-worms.

Symptoms.—In children the effects of this parasite are often marked. Numerous instances of anemia, nervous symptoms of moderate degree, and even chorea are recorded in the literature. That such conditions were due to the presence of the parasite can hardly be doubted in view of their prompt disappearance after expulsion of the worms.

Taenia solium Linnaeus 1758

Synonyms.—*T. pellucida* Goeze 1782; *T. vulgaris* Werner 1782.

The armed human tapeworm, or the pork tapeworm of man as it is often called, is ordinarly from two to three meters long, rarely from six to eight meters. The head is spherical or quadrangular and measures about 1 mm. in diameter. The short stumpy rostellum, often heavily pigmented, bears a double crown of from 24 to 34 hooks in which large and small alternate regularly. The large hooks measure from 160 to 180μ, the small from 110 to 140μ in length. The acetabula are round, prominent and about 0.5 mm. in diameter. The neck is long and slender. About 800 or, at most, 900 proglottids make up the body; the first are very broad and short; at about one meter from the scolex they are square and at the end of the chain, when ripe, they measure 10 to 12 mm. by 5 to 6 mm. The genital pores alternate fairly regularly. The uterus in ripe proglottids has a prominent median stem with from 7 to 10 branches on each side; these branches are heavy, expanded and branched irregularly at the end somewhat in the form of the antlers of an elk. The embryophores are spherical and measure from 31 to 36μ in diameter. Ripe proglottids are generally detached in small groups of five or six, rarely individually, and always evacuated with feces, never between stools.

Diagnostic Features.—The structure of *Taenia solium* is so closely like that of *T. saginata* just described that only the prominent differences need mention. When the head is available it can easily be distinguished by size, shape and especially the crown of hooks. The chain is more delicate, smaller, less muscular and more transparent than that of the beef tapeworm. These characters appear in all of the parts but are difficult to utilize in diagnosis. In sexually active proglottids, one notes the marked difference in size of the ovarian lobes, their oval form and the existence of a smaller accessory lobe in the angle formed by the uterus, vagina, and vas deferens. This lobe is wanting in other species and forms a positive diagnostic feature of *Taenia solium*. Despite the differences noted for ripe proglottids in the form of the uterus and number of its branches, the detached segments are often difficult to name either because they are not full grown, or are broken or distorted; the uterine branching is well brought out by treatment with acetic acid (Fig. 366*B*).

Occurrence.—The adult lives exclusively in man, occupying the anterior portion of the small intestine, though like *T. saginata* its presence may remain unnoticed for a long period. It is readily removed by vermifuges. The name suggests its usual solitary condition, although according to Leuckart this is not the true origin of the designation *solium*. Cases of multiple occurrence are much more frequent than in *T. saginata*. Barrois reported 22 specimens in a single host and Verdun cites a case with 59.

Cysticerus.—The bladder-worm, known as *Cysticercus cellulosæ*, occurs in the muscles and viscera of the pig, producing the condition generally recognized under the name of measly pork. This disease is cosmopolitan and was recognized by the early medical writers though its relation to human tapeworm disease was not demonstrated until the middle of the nineteenth century. The frequency of the bladder-worm in pork has diminished markedly in the last 50 years. The infection of the pig is accomplished by the ingestion of living ova in its food or drink. The oncosphere, released by digestion, follows the same route in its migrations as that already described for *T. saginata*. Once settled in muscles or in viscera it grows rapidly, and at the end of the third month it is ready for transfer to a new host. It enters on a resting stage and waits for the consumption of the flesh by man. At this time it is an oval vesicle about 15 by 7 or 8 mm. in diameter, filled with fluid, into which projects at one point the scolex formed in reverse and showing clearly the suckers and the crown of hooks. While sometimes this bladder-worm degenerates at an early stage or becomes indurated by a deposit of lime, it may on the other hand live long unchanged. In one instance the same specimen living for 20 years in the eye, was observed by the ophthalmoscope. If freed from the cyst formed by the host tissues and placed in warm water (27 to 40°C.), the head evaginates readily and manifests considerable activity. This occurs in the stomach when pork containing living larvæ is digested. The scolex attaches itself in the duodenum, the bladder is lost by digestion and the neck grows out to the full-sized body of the adult. About three months are required for the completion of the growth and the first discharge of ripe proglottids. The development of the bladder-worm in the pig has been produced experimentally many times, also the infection of the human host by feeding living *Cysticercus cellulosæ;* but Brumpt gives evidence that some persons are not susceptible.

Anomalies, though less frequent than in *T. saginata*, also occur and take the same form as those already described for the latter species. One of the most famous was a bladder-worm with three rows of hooks, with 14 to 16 hooks in each; it was discovered in Virginia in the human host and named *Cysticercus acanthotrias* by Weinland, who premised the existence of a corresponding tapeworm, *T. acanthotrias*. Later evidence revealed that it was only a unique variety of *C. cellulosæ*.

Cysticercus cellulosæ has been reported from a considerable number of hosts besides its chief host the pig. As Ransom has stated, most of these reports are doubtful as they rest on single observations, unconfirmed by experiment, and many of them more probably concern other species. As undoubted larval hosts, one may list the dog and also man, a fact which makes this species much more dangerous than *T. saginata*. If by reversed peristalsis, proglottids containing mature embryophores are carried back into the stomach, the oncospheres may be set free by gastric digestion and, following the normal life history, migrate into the tissues and produce the full-grown bladder-worm. These have been found in muscles and in connective tissue, and in such locations are relatively innocuous. But unfortunately they seem to reach frequently the eye and the brain, with more serious results. In a series of 907 records studied by Vosgien* the parasites were located in a single organ in 807 cases and formed a generalized infection in only 100 cases. In the 807 cases of localized cysticercosis the location of the parasite was as follows:

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* Vosgien, Le cysticercus cellulose chez l'Homme, etc. Thése, Paris (1911).

	Cases	Per Cent.
Eye and adnexa	372	46
Nervous system	330	41
Skin and subdermal tissue	51	6
Muscles	28	3
Other organs	26	3

Cases involving the nervous system are evidently of serious significance. Of the 330 cases cited, Vosgien listed 279 in the brain and meninges and 41 in the cerebral ventricles. In these places the bladder-worm is not surrounded by a cyst such as is produced in other locations by the host tissue; hence it tends to grow and assume a branching form, designated the *Cysticercus racemosus*. This produces effects similar to those of brain tumor and has frequently caused sudden death without suspicion of the presence of the parasite. Diagnosis is evidently difficult and prognosis depends clearly on the exact location of the bladder-worm, but cerebral cases almost always terminate fatally.

Distribution.—The distribution of *Taenia solium* accords with that of the pig and is definitely related to the consumption of pork, being most frequent where pork products are used in uncooked or partly cooked condition. In Europe from 50 to 70 years ago, it was the most common human cestode but has grown much less abundant in recent years. Although most texts refer to this species as common here, it is in fact very rare in North America. Among many hundred specimens sent to me for determination in the last 30 years, I have never found one *Taenia solium*. It has been recorded very rarely by others and early statistics are misleading because of confusion with *T. saginata*. Inspection at various places in the U. S. of 1,000,000 hog hearts for the larval *Cysticercus cellulosæ* revealed less than 25 infected; but at Fort Worth (Texas) several are commonly found each week and hogs from the San Luis valley are often infected. The tapeworm is said to be frequent in Mexico and some parts of Central America. In Portugal, where it seems most abundant now, Bettencourt found it in 63 per cent. of all cases of Taenia submitted to him.

Cases in Children.—Cases of infection with *T. solium* in children are reported from Europe. Thus Gautier* reports that a boy, aged five, with very definite symptoms of meningitis (headache, vomiting, rigidity of neck, positive Kernig's sign, albumen in cerebrospinal fluid and increase of cells up to 400 per cu. mm.) was relieved of *T. solium* by treatment. Thereupon the symptoms rapidly improved and the child was discharged from the hospital on the fifth day. No cases in children are reported from North America.

Other Species of Taenia.—Several other species of this genus have been described from man but are rare and possibly represent in part only unusual variations of the common species. Although they are not known to be in any way related to children they may be significant in some regions, and furthermore it is important to secure exact data in order to avoid confusion with more common species.

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* Gautier, P., Un cas de méningite vermineuse. Bull. et mém. soc. méd d. hôp. de Par., xlvii (March 22, 1923), pp. 429–432.

Taenia confusa Ward was described from specimens obtained in Nebraska in 1896. It was recently reported from Texas by Chandler. The species is characterized by the extraordinary length of the ripe proglottids and by their shape. It has been said to be a relic of an aboriginal species which has all but entirely disappeared from the continent. It should be looked for in the plains region and westward.

Various writers have reported the possible or occasional presence in man and particularly in children, of the dog tapeworms, *Taenia marginata* and *T. serrata*, and the cat species, *T. crassicollis.* But several experimenters, most recently Hall,* have demonstrated on themselves the impossibility of getting the bladder-worms of Carnivora to settle down in the human intestine.

Taenia infantis Bacigalupo 1923 was described from a specimen obtained from a child of five years in a Buenos Aires hospital. Though it was very much like *T. crassicollis*, the author considered it a new species.

Taenia coenurus Küchenmeister 1854 is a parasite of the dog in the adult condition. The larva, *Coenurus cerebralis* of the sheep, develops only in the brain, where it gives rise to the so-called "gid." In two cases this larva has been found in the human brain.

GENUS ECHINOCOCCUS Rudolphi 1801

Very small (3–6 mm. long), only 3 or 4 proglottids, last one alone ripe. Scolex with double crown of 28 to 50 hooks, 40 to 45 and 30 to 38μ long. Eggs ovoid, 21 to 30 by 32 to 36μ. Embryo about 25μ long.

Adult in intestine of dog and cat. Larva encysts in connective tissue in a large number of hosts.

Only one species is known as an adult (*E. granulosus*), but a second is identified in the bladder-worm stage (*E. multilocularis*). In Australia the adult from the native dog is said to be 30 mm. long; this would seem to belong to a different species as yet undescribed.

Echinococcus granulosus (Batsch 1786)

Synonyms.—*Taenia echinococcus* v. Siebold 1853; *Echinococcifer echinococcus* Weinland 1861; *Vesicaria granulosa* Schrank 1788.

Structure.—The adult is small, 2.5 to 5 or 6 mm. long, with only three or four proglottids, the last of which measures when ripe 0.6 by 2 mm. The scolex is 0.3 mm. broad with a prominent rostellum, carrying in a double row 28 to 50 hooks which vary notably in size and form. The uterus is median with short rounded lateral diverticula; it contains from 400 to 800 eggs. The embryophores are oval, 32 to 36 by 21 to 30μ.

The adult is a widely distributed parasite of the dog and the wolf, also of the jackal and the dingo. It was long regarded as an immature form by virtue of its small size. It was produced experimentally by von Siebold, who fed hydatid cysts to sheep. It occurs in large numbers, as will be clear from a study of the life history. The larval form, echinococcus or hydatid cyst, occurs normally in a large number of mammals and a few birds. Among larval hosts must be listed man.

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* Hall, M. C., Experimental Ingestion by Man of Cysticerci of Carnivore Tapeworms. Jour. Parasitol., i (Sept., 1914), pp. 42–44.

Formation of Hydatid Cysts.—Leuckart followed the development by feeding the adult tapeworms to suckling pigs. The oncospheres come to rest most often in the liver. Growth is slow and in one month the larva has grown to a solid sphere, measuring only 0.25 to 0.35 mm. in diameter and enclosed in a connective tissue cyst produced by the host. The entire structure forms a nodule in the liver scarcely 1 mm. in diameter. At two months the size is doubled, fluid has collected in the cyst, and in it one can readily distinguish the thick external lamellar cuticula and the granular, internal germinative membrane. At five months the vesicle is from 10 to 12 mm. in diameter and the interior is still sterile. To this condition the name Acephalocystis has been applied and some specimens never advance beyond this stage. Some months later there usually appear protuberances on the germinative membrane (endocysts). Such a growth develops rapidly into a brood capsule in which the endocyst is external and the cuticula internal. These may become free and float about in

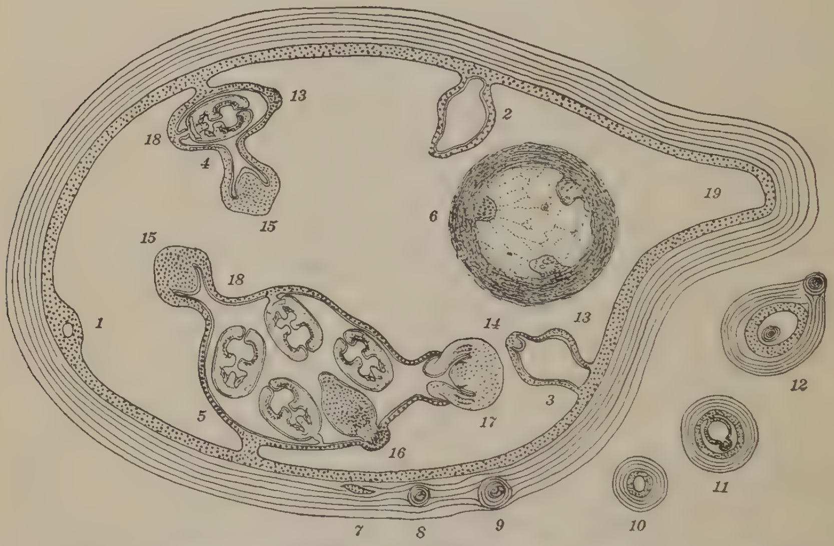

FIG. 367.—Diagrammatic section of Echinococcus bladder. 1, origin of a brood capsule; 2, 3, 4, further stages in its development; 5, fully developed capsule; 6, endogenous daughter cyst formed from brood capsule; 7, origin of an exogenous daughter cyst; 8, 9, 10, 11, its further development; 12, an exogenous daughter cyst forming an exogenous and an endogenous cyst of the third generation; 13, origin of a scolex as a minute elevation in the wall of a brood capsule; 14, its delimitation by a shallow internal groove; 15, later stage; 16, same as last, but invaginated; 17, the enclosing of the papilla by a second outer furrow; 18, a fully developed scolex with head inverted. Original.

the interior of the mother cyst when, however, a cuticula is formed on the exterior and disappears within. Such free daughter cysts may be formed in the wall of the mother cyst. As they grow and burst they may fall into the original cyst cavity and give rise to the endogenous type. If they burst and develop outside the mother cyst, there originates the exogenous type. A third generation of cysts may arise within the second. Any or all of the cysts may remain sterile but ordinarily heads are formed on the brood capsule or secondary cyst. The growth of such heads may be followed in figure 367. On its completion the head is left projecting into the cavity of the brood capsule. Suckers and hooks are formed so that the structure appears as an inverted scolex. As from five to 10 or even 34 heads may be developed in a single daughter cyst, the total number in one echinococcus may reach into the thousands.

The form of the hydatid cyst varies greatly and the different types have been named and also regarded by some as distinct species. The formation of evaginations in the wall lead to the type known as *Echinococcus racemosus.* The type designated *E. multilocularis* known also as an alveolar colloid was interpreted as a colloid cancer until Virchow demonstrated its hydatid origin. Scolices and hooks are rare and entirely wanting in some 40 per cent. of cases.

Distribution.—In the United States the hydatid is rare in man. The first case was recorded in 1819. Statistics* have been compiled of 334 cases, most of which were certainly introduced, but a goodly number must have been acquired here. About 91 per cent. of the patients were foreign born and only 9 per cent. native; but it is impossible to determine whether the latter had traveled abroad or what part of the former might have acquired the disease in this country.

The seat of the parasite is preeminently the liver. Of 1806 cases I listed in 1901, the liver claimed 1011, the lung 147, the kidney 126, the spleen 42, the circulatory apparatus 53, the cranial cavity 91, the peritoneum 62, the pelvis 75, and the female genitalia 60. Vegas and Cranwell cite 2027 cases with 75 per cent. in the liver, 8 in the lung, 6 in the muscles, 2 each in the kidney and the spleen and the remainder scattering. In Magath's 93 cases in the United States since 1902 69 cases concerned the liver, 10 the peritoneum, 4 each the lungs, kidney and omentum, and in 13 cases cysts were scattered in other organs; in all 104 organs affected.

The hydatid disease of the unilocular type is most common in Iceland, and moderately frequent in Italy, Greece, Russia and Germany; it occurs also in France, England and Armenia. It is very abundant in Argentina, Uruguay, New Zealand and Australia. The multilocular type occurs chiefly in two definitely limited areas; one includes Switzerland with South Germany and the Austrian Alps; the other involves southwestern Russia and Siberia. W. R. Smith maintains that it is a very common parasite in Australia (Med. Detroit, ix (1905), p. 729) and supports strongly the view that it is the larval stage of a species different from *E. unilocularis*.

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* Magath, T. B., Echinococcus disease: Etiology and laboratory aids to diagnosis. M. Clinics N. America, v (Sept., 1921), p. 549.

Incidence in Children.—In general one may say that hydatid disease is rare in children. Only two of the 93 patients listed by Magath are as young as 10 years; others state that hydatid cysts are rarely met with in patients below the age of 20 years, whereas after that period its frequency increases regularly. Magath mentions that in South America the percentage of infection in children is high, and in Argentina 26.2 in every 100 cases occur in children under 4 years. But Greenway (J.A.M.A., lxxix (Dec. 9, 1922), p. 2019) protests, stating that both the data and the suggestion of a close and insanitary association of children and dogs are incorrect. Among 2470 patients he gives 11 per cent. less than 14 years and 0.54 per cent. less than four years. But other authors mention numerous cases. Thus among children Cranwell and Vegas (from whom in fact Magath's figures of 26.2 per cent. were quoted, although the age limit, by a typographical error, appears as four instead of 14) note eight patients below three years out of 419 cases; Legos Garcia 12 in 269 cases; Pena four in 149, and others report one case of two years or less. In one case a hydatid cyst of the orbit was first noticed at the age of three months. In a study of the hydatid cysts of the liver in children published in Paris in 1867, Pontou contended that hydatid cysts appear rare in children only because they are unrecognized, owing to the slowness with which they develop and the absence of symptoms during the initial phases of their growth. This view has been critically investigated in an exhaustive series of studies on hydatid disease in children made by Dévé.* He reaches the conclusion that although the disease reveals itself ordinarily among adults, its germ is more often contracted in childhood and even in infancy. The age at which the cyst is removed should not be confused with that at which the infection is acquired. Indeed, cases of undoubted prenatal infection are on record.

In Montevideo, Zerbino has recently investigated the views of Dévé regarding the relations between the hydatid cyst of the child and that of the adult. A comprehensive review of all published data shows that 27 per cent. of 1511 cases were recorded from patients less than 15 years of age. The maximum frequency increases up to about 25 years and then decreases steadily. The relations between age and localization of the cyst are represented in a table.

Zerbino reaches the following general conclusions: (1) The hydatid cyst is pre-eminently a malady of infancy, youth, and early adult life, while it is exceptional in older persons; (2) the major frequency falls between 20 and 25 years but early childhood constitutes a most favorable period, with a frequency of about one-third of all cases; (3) infection may take place at all ages undoubtedly depending on exposure to favoring conditions, for which the maximum period in infancy or early

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* Dévé, F., 1918. L'Echinococcose de l'enfant. Arch. med. enf., xxi (May, 1918), pp. 225–245.

Table 7.—Localization of Hydatid Cysts According to Age

Age, years	Liver	Lung	Liver and lung	Spleen and lung	Spleen	Liver and spleen	Kidney	Brain	Multiple abd. cysts	Single abd. cysts	Subcut.	Pancreas	Bones	Pleura	Ovary	Liver and brain	Liver and kidney	Thyroids	Mediastinum	Others
0– 5	25	4	3	..	..	..	..	3	2	1	..	..	..	..	..	1	2			
6–10	57	26	7	2	..	..	3	2	2	1	1	..	..	..	..	..	1			
11–15	60	21	4	..	..	1	1	4	..	..	..	..	..	..	..	..	..	1		
16–20	50	25	..	..	1	..	1	..	1	3	2	..	1	..	..	..	..	1	..	
21–25	82	24	..	..	1	..	3	..	7	2	1	1	2	1	3					
26–30	50	21	..	..	..	..	2	..	3	1	2	1	..	1	1	..	..	..	..	1 uterus
31–40	74	25	1	..	2	..	1	..	2	..	1	1	1	1	..	..	..	..	1	1 parotid
41–50	34	12	1	..	..	..	2	..	..	1	2	..	..	..	..	..	..	..	1	
51–60	9	5	..	..	..	..	1													
61–80	2	1																		
Total.....	443	144	16	2	4	1	14	9	17	9	9	3	4	3	4	1	3	2	2	

childhood, and the multiplication of the infection is more frequent in childhood owing to the degree of exposure to contamination. The frequent contamination of children is but to be expected from their intimacy with dogs, disregard of hygienic procedure and inattention to the condition of food. The age of dirty hands and the time of walking on four feet, *i.e.*, infancy, is also the period of most intimate association with the dog and with places contaminated by it. Clinical records in hydatid infested areas show that children with cysts nearly all come from the country. In Greenway's most recent statistics 56 per cent. of cases came from the region about Buenos Aires and only 30 per cent. from within the city limits.

It is important to notice the localization of hydatid cysts in the child as compared with the adult. Dévé gives the following table, showing the percentage based on number of cysts, not number of cases.

Table 8.—Localization of Hydatid Cysts

In the adult (over 15 years old)	Per Cent.	In the child (under 15 years old)	Per Cent.
1. Liver	76.6	1. Liver	76.2
2. Lung	9.4	2. Lung	11.1
3. Muscle and connective tissue	5.2	3. Brain	4.3
4. Kidney	2.3	4. Muscle and connective tissue	3.2
5. Spleen	2.1	5. Kidney	1.2
6. Bone	0.9	6. Spleen	1.1
7. Orbit	0.7	7. Orbit	1.0
8. Brain	0.6	8. Bone	0.1
9. Divers organs	2.2	9. Divers organs	1.8

It is striking that the brain which in the adult takes a low rank as a location for hydatid cysts occupies third place in the child. For evident reasons, cysts in the brain nearly always manifest their presence at an early age, while in the other organs they may persist for years without invoking serious trouble. The same applies to orbital cysts whereas the reverse is true of hydatid cysts in the bone.

Diagnosis.—The early and accurate diagnosis of hydatid disease is evidently of great importance. The older method of puncture and micro-examination of the fluid to find hooklets of daughter cysts is not without danger, as was pointed out long since. It is being superseded by various laboratory methods. The growth of the organism results in the formation of specific antibodies which manifest their presence clearly in a complement fixation test, in a precipitin reaction test, in the Abderhalden reaction, in an intradermic reaction, and in a cutaneous test. These are fully described by Magath who says there is perhaps no other disease which gives so clear-cut a reaction in so many different tests as does echinococcosis. The symptoms are referable to the organ affected.

General Outlook.—In general the prognosis of hydatid disease is notably more favorable in the child than in the adult except in such special cases as the brain cysts, in which the outcome is always fatal. Of the disease in general it may be said that it is the most fatal zooparasitic malady. In some regions, notably South America it is rapidly increasing. Greenway states that from 1910 to 1922 it increased in frequency in cattle from 5 to 15 per cent. and in sheep from 5 to 30 per cent. While the increase in human cases will for evident reasons lag behind that in domestic animals, it will follow surely at an interval of 15 to 20 years. The only successful method of combating it lies in preventing the consumption of offal by dogs and in the extermination of the homeless and wandering curs that, in their distribution of the germs of this and of other diseases, constitute a serious menace to the health of the human race in many communities.

Treatment.—Simple puncture of the echinococcus cyst is uncertain and dangerous. Total extirpation by surgical interference is the preferred procedure. Care is taken to remove the cyst entire without rupture or loss of contents. Dévé advises the injection of 1 per cent. formol solution into the cyst before the operation; he also recommends operating at the earliest possible age since the cysts grow and proliferate with years so as to render their removal more difficult and dangerous. Neither vaccination nor radio-therapy exert any influence upon the growing cysts.

FAMILY HYMENOLEPIDIDAE Railliet and Henry 1909

GENUS HYMENOLEPIS Weinland 1858

Synonym.—Diplacanthus Weinland 1858.

Scolex small; rostellum retractile, armed with small hooks not hammer-shaped; suckers unarmed. Genital pores on left margin. Three testes in each proglottid. Uterus sacculate, filling entire ripe proglottid. Egg with two membranes, widely separated. Larva a cercocystis or staphylocystis. Many species in mammals and birds.

Hymenolepis nana (von Siebold 1852)

Synonyms.—*Taenia murina* Dujardin 1845; *Taenia nana* von Siebold 1852; *T. aegyptiaca* Bilharz 1852; *Diplacanthus nanus* Weinland 1858.

The dwarf tapeworm (Fig. 368) is usually from 10 to 25 mm. in length, rarely 40 mm.; the breadth is from 0.5 to 0.75, rarely 0.9 mm. The scolex is spherical, 0.25 to 0.3 mm. in diameter; the retractile rostellum is short, thick and armed with a single circle of from 24 to 30 hooks 15 to 18μ long. The suckers are relatively large (80μ in diameter). The neck is long and only half as broad as the scolex. The proglottids number from 100 to 200; the first are very short, they increase gradually in size but those near the posterior end measure only 0.7 to 0.9 mm. by 0.15 to 0.20 mm. The external egg membranes measure 60 to 77μ, the internal 30 to 40μ and the onchosphere 25 to 30μ in diameter. The poles of the inner membrane are provided with groups of long filaments. Detached segments are broken up by digestion and one finds free eggs in feces of the host (Fig. 346).

Apparently infection is exclusively between members of the human species. The development of the rat parasite, which was formerly designated *H. murina* renamed *Hymenolepis fraterna* by Stiles (1906), is recorded here because of the apparent relationship between it and *H. nana* and the total lack of information concerning the development of the human parasite.

Rat Parasite.—Grassi in working out the life history in young white rats, found that when eggs were ingested the oncospheres were set free in the intestine and invaded the villi in the last few centimeters of the small intestine. In about 100 hours each had developed to a bladder-worm, had ruptured the villus and had attached itself to the intestine. The scolex alone grew and in 15 days gave rise to a full-grown adult worm. This seems to be the only method of development. Such auto-infections would lead soon to an intensive parasitism which, unless it were self-terminating, would shortly destroy the host. In other words, this life history explains the multiple infection which is so common in this species, but

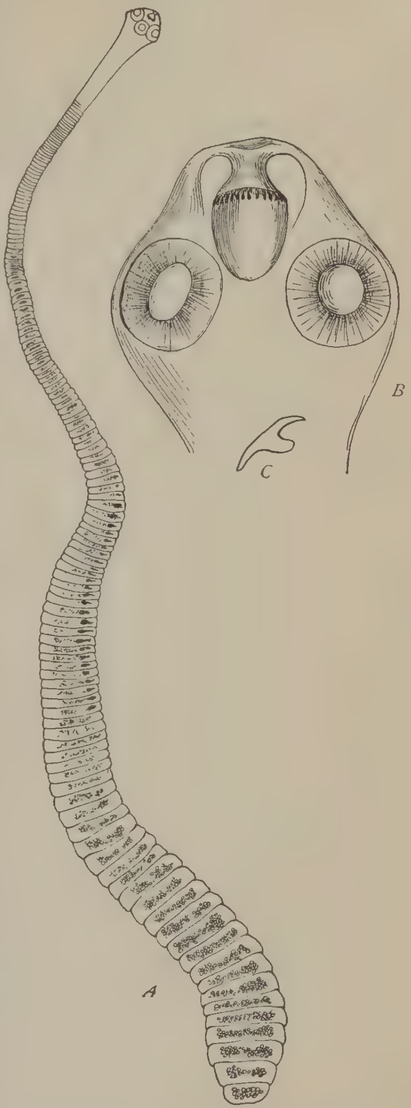

Fig. 368.—*Hymenolepsis nana.* *a*, entire worm, ×9; *b*, scolex with rostellum retracted, ×100; *c*, hook, ×600. (After Leuckart.)

it throws no light on the absence of early fatility to the host. On this point more will be said later.

Human Species.—The parasite from man was long regarded as identical with one from the rat but many failures to infect by feeding eggs from the other host have thrown doubt upon the identity of the two forms. The question is still *sub judice* even though differences in adult structure have not yet been found. This complex question has not been much cleared up by very recent experiments. Woodland (Parasitology, xvi (Dec. 12, 1924), p. 424) was partially successful in infecting Hymenolepis-free mice with eggs of the human *H. nana*. He also offers further evidence of the identity of rodent and human species. But Joyeux calls attention to the difficulty of this experimental transfer whereas *H. fraterna* is easily transferred. He states also that *H. nana* is limited to the tropics whereas *H. fraterna* is cosmopolitan in distribution.

In the experiments of Calandruccio on man and of Yoshida and Saeki on a girl five years old, the development was direct, but the exact manner or place in which the cysticercoids of the human parasite developed was not determined. The problem remains unsolved and its importance demands attention.

The adult dwarf tapeworm of man inhabits the distal portion of the ileum in considerable numbers, even up to 4000 or 5000 in a single host. The latter condition is easily understood if man is at once both final and intermediate host, as facts just discussed would indicate.

Distribution.—The parasite was formerly regarded as very rare. It was discovered in Egypt by the famous surgeon Bilharz in 1851; he found it in enormous numbers at a necropsy. Since then it has been reported from nearly all parts of continental Europe. It is sporadic in the northern regions and common in the south and east. Records have come also from Siam, Japan, the Philippines and many other countries, so that it may rightly be regarded as cosmopolitan in distribution. Yet it is important to avoid errors due to earlier citations of the rat parasite. The distribution of *H. nana* of man and *H. fraterna* of the rat apparently differ. The latter has been recorded everywhere over the world. *H. nana* is probably limited to subtropical countries and some adjacent territory such as the circum-Mediterranean region, Asia, Africa and the East. Joyeux found it only five times in France, whereas from 20 to 80 per cent. of rats in that country are infected with *H. fraterna*. Bettencourt calls *H. nana* the commonest human cestode in Portugal, 33 out of 503 children examined being infected. Carini and Mastrangioli reported 11 cases in Brazil from 1908 to 1912; Stewart eight cases in adults in Hong Kong; Waite 51 cases in North Queensland; Hasegawa and Yamanonchi five cases in Tokyo.

Occurrence in U. S.—Spooner in 1873 reported the first case in the United States but this was probably the next species, and the first certain case was described in 1885. Since then several thousand have been put on record, almost all of them in the last 20 years. In 1904

Ransom* published a monograph on this parasite and its congeners, listing 129 cases for this species and giving a thorough account of its structure, distribution and effects. For the United States Ransom reported 25 cases, all but one of which had been recorded since 1902, and Stiles predicted that this would prove to be the most common intestinal parasite in the United States. By 1910 the number of cases had reached 33, but in that year Schloss reported 20 cases among 280 children who had been examined for intestinal parasites. On the other hand, among these children were only five cases of *Taenia saginata.* A series of examinations in the South demonstrated the presence of *H. nana* in 1004 cases among 62,785 persons examined, in contrast with only 10 *Taenia saginata.* In New Orleans de Buys found *H. nana* in 55 cases among 595 children from seven different institutions, an incidence of 9.25 per cent., which is noteworthy also because no other tapeworms were found. Among 1200 American soldiers who had been overseas were seven cases, and among 300 home service men not one. On the other hand 230 cases were reported from 35,000 white and black troops at Camp Zachary Taylor Kentucky. In this same group *Taenia saginata* was found 12 times. These facts indicate how extremely common this species is as an intestinal parasite in the United States, especially throughout the South. They indicate further a much larger incidence among children than among adults, either in civil life or service. Additional cases are constantly being reported.

Incidence.—In general, infection with this species is distinctly related to unfavorable hygienic conditions and to personal carelessness and indifference to sanitary procedure, since the parasite is rarely found in adults, and such as harbor it are usually of defective mentality or aged and neglected. The species is pre-eminently a parasite of infants and young children, in whom, though it is the smallest of human cestodes, it plays an important pathogenic rôle. Its frequency in many parts of the world may be partially represented by a tabular review.

This is given in Table 9 on page 996.

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* Ransom, B. H., An account of the tapeworms of the genus Hymenolepis parasitic in man, including reports of several new cases of the dwarf tapeworm (*H. nana*) in the United States. U. S. Hyg. Lab. Bull. No. 18 (September, 1904).

Table 9.—Frequency of Hymenolepis Nana

Country	Class of persons examined	Per cent. infected	Authority cited
Sicily	Infants	10.0	Grassi
Portugal	Infants	6.5	Bettencourt
Spain	Infants		
Macedonia	Children	7.0	Joyeux
Algeria, South Oranais	Children	frequent	Foley
Alger	School children	20.0	Soulie et Derrieu
Duzerville	Adults	1.5	Parrot
Upper Guinea	....	5.0	Joyeux
Japan (Loochoo Isl.)	....	3.6	Y. Hoki
Australia, Queensland	Orphanage	18.0	Maplestone
United States (South)	All ages	1.5	Wood
Florida	Infants	39.0	Wood
Texas	Orphanage	32.6	Frey
Texas	Adults	0.5	Judkins
New York	Children	7.0	Schloss
New Orleans	Children	2.7	Bass and Gage
New Orleans	Children (institutions)	9.3	De Buys

Life History Unusual.—The general occurrence of the disease among inmates of the same institution or in several members of the same family has been noted again and again by various observers (Grassi in 1887, Schloss in 1910, Carpenter, de Buys, Goldman and Chandler more recently), supporting the view that an intermediate host is not necessary. Furthermore experimental infestations of a child of four years were apparently successfully conducted by Saeki in Japan. If man can serve as both final and intermediate host, the ingestion of a few ova in polluted drinking water, on dirty hands with contaminated uncooked food materials or in some such accidental fashion, might bring about a multiple or mass infection by virtue of later increase through multiplication within the host.

By the administration of a vermifuge Goldman secured in certain cases small tissue fragments with two to eight heads of *H. nana* in each. The rostellum, hooklets, four suckers and caudal appendix were easily seen, but no segments were visible. Goldman considered these were the cercocystis stage of the dwarf tapeworm.

Diagnosis.—The tapeworms are too small to be seen with the naked eye unless large numbers are present in the stool, as may be the case after treatment. A microscopic examination is accordingly necessary and usually results in finding the characteristic "ova" enclosing the six-hooked embryos (oncospheres). Bass and Gage advise centrifuging to secure the eggs.

Symptoms.—Among the symptoms asssociated with the presence of *H. nana* are noted: Abdominal pain or tenderness and diarrhea most frequently; anemia, dizziness and headache. Various nervous disturbances and even epilepsy have been observed. These symptoms uniformly disappear with the removal of the parasite. In a necropsy report, Imes records bloody extravasations on the mucous membranes of the ileum which he thought indicated points where the tapeworms were attached. One of Goldman's heavily infected cases showed the presence of blood in the feces. Eosinophilia is a constant condition in cases of infection with the dwarf tapeworm, and ranges from two to nine per cent., being six per cent. or more in cases with definite symptoms, and higher in children than in adults.

Treatment.—The use of male fern is ordinarily followed by immediate amelioration of the symptoms. While a single dose usually effects a complete cure, other cases are more resistant and eggs are found in the stools after several treatments. I have found specimens of *H. nana* among hookworms obtained in Kentucky by thymol treatment; the presence of the tapeworm was neither recorded nor suspected.

Hymenolepis diminuta (Rudolphi 1819)

Synonyms.—*T. diminuta* Rud. 1819; *T. leptocephala* Creplin 1825; *T. flavopunctata* Weinland 1858; *T. varesina* E. Parona 1884; *T. minima* Grassi 1886.

This species is from 200 to 600 mm. long and from 3 to 5 mm. broad. The scolex is small, claviform, and somewhat flattened at the apex; the rostellum is rudimentary, unarmed and scarcely protractile. The suckers are small and the neck is short. The proglottids are short and indistinct at first, increasing gradually to a maximum, near the end of the chain, of 3.5 mm. by 0.66 mm. (Fig. 369). The round or oval eggs measure from 60 to 86μ in external diameter. Both the membranes are thin; the internal membranes have distinct polar knobs but no filaments; the oncosphere measures 36 by 28μ and it hooks are 11μ long (Fig. 371). Terminal proglottids are broken up after being detached, so that free eggs are found in feces of the host.

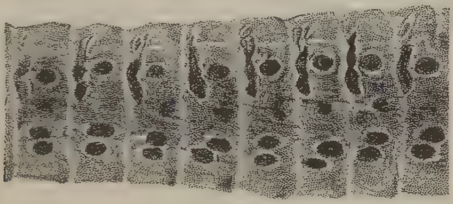

FIG. 369.—*Hymenolepis diminuta.* Portion of chain. ×250. (After Fülleborn.)

In structure this species is substantially like *H. nana* but it is easily distinguished by the measurements. Dwarf proglottids, which are sterile, occur often at intervals in the chain and are conspicuous features. The oncosphere develops in the body cavity of various insects, most commonly the meal moth, *Pyralis farinalis*, but also in the earwig (Anisolabris), two beetles (Akis and Scaurus), and was found by Nickerson (Science, n.s. xxxiii; 271) at Minneapolis in two thousand-legged worms (*Julus* and *Fontaria virginia*). Joyeux found experimentally that the adult flour beetle (*Tenebrio molitor*—not the larval meal worm) and fleas were the most favorable intermediate hosts. Cockroaches (Periplaneta, Blatta) could not be infected. Feeding rats with viable eggs of *H. diminuta* failed to produce an infection. However, by feeding infected insects, the adult has been developed experimentally in white rats and in man. In the human host ripe eggs appeared in the feces 15 days after ingestion of the infected insects.

Relation to Food.—The adult is the common parasite of rats and mice and is probably cosmopolitan with its hosts. One-fifth to one-half of all rats examined in the country harbor it. It inhabits the distal portion of the small intestine and, when abundant in a single host, apparently induces cachexia. The close association of its intermediate hosts with human food explains readily the occasional and widely distributed cases in man. The consumption of infected insects in uncooked or poorly prepared food, *e.g.*, cockroaches or meal moth larvæ contained in cereals, or caught in dough and eaten in rapidly cooked biscuits, is undoubtedly responsible for cases of human infection. In contrast with *H. nana* this species is rather rare in man. Ransom compiled records of 12 cases. Riley and Shannon* have expanded this list to include 61 cases in all. It is important to note that the number of worms in each human case is relatively low, and varies from one to four. This fact suggests the casual character of the parasitism in man.

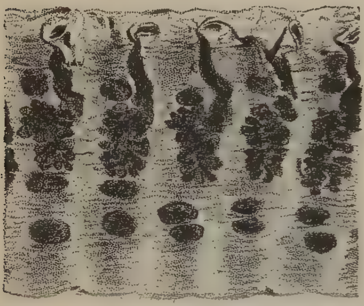

FIG. 370.—*Hymenolepis diminuta.* Older section of chain. ×250. (After Fülleborn.)

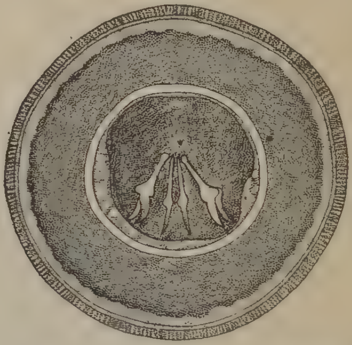

FIG. 371.—Embryo of *Hymenolepis diminuta* enclosed in egg membranes. ×750. (After Fülleborn.)

Geographic Distribution.—Known cases are distributed geographically as follows: Brazil, 19; United States, 17; India, 8; Italy, 7; Japan and Nicaragua, 3 each; German East Africa, 2; and one each for Argentine, Belgium, Cuba, Grenada, Martinique, and the Philippines. Various authors have pointed out the likelihood of error in routine examination when eggs of this species are reported as of the more common species *H. nana.* Accuracy would raise the totals given above to a considerable extent in the opinion of Riley.

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* Riley, W. A., and Shannon, W. R., The rat tapeworm, *Hymenolepsis diminuta,* in man. J. Parasit., viii (March, 1922), p. 109.

Age Incidence.—The age distribution of these cases interests us greatly here. The youngest was less than nine months old; three others were 17, 19 and 20 months old. At or below three years of age are recorded eight further cases. Two cases each at four, seven and eight years, one each at nine and eleven, and two each at 12 and 13 years. Five others are entered only as "children," making a total of 29 such cases as against 15 cases in "adults" and 22 cases in which no age data were given.

American Cases.—The first American case in a child, aged 19 months discovered by Palmer in Boston in 1842, was described in 1858 by Weinland.* In 1884 Leidy recorded it in Philadelphia, and Packard again from that city in 1900. An Arkansas case was published by Deadrick in 1906 and one from Minnesota by Nickerson in 1911. Later records have come from Indiana, Nebraska, the District of Columbia, Louisiana and Virginia. Lucké did not find it once even in 35,000 white and colored troops examined at Camp Zachary Taylor, Kentucky, nor was it discovered by Kofoid, Kornhauser and Plate in examinations of 1200 overseas and 300 home service troops.

In contrast with *H. nana* are the mild infections with correspondingly mild symptoms. However, recently reported cases have been associated with rather marked symptoms. The parasite is readily diagnosed from the occurrence of its eggs in the feces; these are easily distinguished microscopically from those of the dwarf tapeworm of man by the size of the ova (Fig. 371) and the absence of polar filaments on the internal egg membranes which are conspicuous in ova of *H. nana.* The adult cestode is readily expelled by anthelmintics. At times it has been removed by cathartics and in one case it was reported to have come away without the administration of drugs.

Very recently Butka† described a case in a boy of 16 months in Los Angeles, who was brought to the hospital because of hunger, loss of weight, restlessness and irritability.

FAMILY DIPYLIDIIDÆ Lühe 1910

GENUS DIPYLIDIUM R. Leuckart 1863

Of moderate size. Scolex with retractile rostellum armed with several annular rows of small alternating hooks, shaped like rose-thorns. Suckers unarmed. Sexual organs double in each proglottid with genital pores lateral on both margins. Testes numerous located in alveoli. Uterus, at first reticulum surrounding testes, later expanding into egg-filled sacs which, as testes atrophy, fill empty spaces. Ripe proglottids with characteristic egg capsules filling space within lateral excretory canals. Eggs with double transparent membranes. Larva cysticercoid.

Dipylidium caninum (Linnaeus 1758)

Synonyms.—*T. moniliformis* Pallas 1781; *T. cucumerina* Bloch 1782; *T. elliptica* Batsch 1786; *Dipylidium cucumerinum* Leuckart 1863.

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* Weinland, D. F., 1858. Human Cestoides. An Essay on the Tapeworms of Man. Cambridge, Mass. 93 pp. 12 figs.

† Butka, H. E., Infestation with *Hymenolepis diminuta* (rat tapeworm), J.A.M.A., lxxxii (March 15, 1924), p. 875.

The double-pored dog tapeworm measures 150 to 350 mm. in length with a maximum width of 1.5 to 3 mm. The small rhomboidal scolex varies in size with the state of contraction. It carries a retractile, club-shape rostellum 185μ long by 110μ wide, armed with three or four rows of small hooks shaped like rose-thorns and varying in length from 15μ in the first row to 6μ in the last. These hooks are extremely caducous so they are at times almost entirely wanting. The suckers are elliptical, and the neck very short and slender. The first proglottids are very short, later they are trapezoidal and finally longer than broad. In ripening they assume the form of melon seeds and for more than half the length of the chain are loosely attached to adjacent segments. Two sets of the reproductive organs, on right and one left, are present in each proglottid (Fig. 372). The spherical eggs, from 35 to 40μ in diameter, are gathered in groups of 8 to 15 into a single uterine capsule. In the living worm these proglottids have a distinct rose tint which disappears in preserving fluids. The eggs are spherical, from 43 to 50μ in diameter; the oncosphere 30 to 36μ. The adult is a very common parasite in the small intestine of the dog and cat, especially in lap dogs and house dogs. The larva, *Cryptocystis trichodectis,* lives in the body cavity of the dog louse and dog flea.

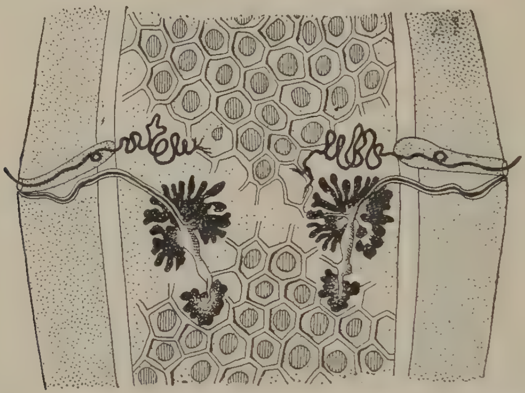

FIG. 372.—Sexually mature proglottid of *Dipylidium caninum.* Magnified. (After Neumann.)

Prismatic and doubly fenestrated specimens are common anomalies, and individuals have been described with four sets of reproductive organs in an apparently single proglottid. The parasite inhabits the small intestine of its host. Ripe proglottids emerge from the anus spontaneously as with *Taenia saginata* of man. They are often seen crawling over the surface of the body of a dog and are crushed by the dog's movements, so that the eggs are eaten by the dog lice (*Trichodectes canis*) and dog fleas (*Ctenocephalus canis*) or even by the human flea (*Pulex irritans*). The fleas are infected only in the larval stage, according to Joyeux, and yet the oncosphere does not develop fully until the flea becomes adult. The fully grown larva of the parasite is known as a cryptocystis. When dogs are irritated by the bite of the fleas and destroy those pests, it is easy to see how they infect themselves by swallowing at the same time the larval parasite.

Cases in Man.—The first case of the adult parasite in man was recorded by Linnaeus. Within recent years its presence in the human host has been signaled with increasing frequency. R. Blanchard* analyzed 76 cases recorded from man, and since then additional records have raised the total considerably.

Among the 81 accurately recorded cases of this parasite in man, 26 or more than 32 per cent. were reported from children under six months. More than two-thirds of the total number were less than three years old. Three-fourths were less than four years old and only 10 per cent. were more than 20 years old. This striking situation is due to the intimate association of infants with pet dogs and cats, which in view of the development of the larval stages of this parasite in the dog and cat flea gives frequent opportunity for transfer to the child. Probably transfer of parasites in infective stages takes place on the tongue of the dog, utilized so constantly in affectionately caressing its infant companion. The lack of care manifested by every infant in the selection of articles conveyed to the mouth is certainly also a contributing factor in the situation. The human host may also be infected by chance contamination of food with infected lice and fleas. Younger children pay little or no attention to the condition of food or drink, or to the cleanliness of pet animals with which they are playing. Such pets often help themselves to food set out in dishes for an infant or a young child and have thus opportunity to contaminate the food or the dish. One can hardly deplore too strongly the habit of fondling closely and kissing household pets; of all these small dogs are the most constant carriers of this parasite. Table 10 groups cases according to the recorded ages of the human host.

TABLE 10.—CASES OF DIPYLIDIUM CANINUM

AGE OF HOST	NUMBER OF INFECTIONS
5 weeks to 6 months	28
7 to 12 months	9
13 to 24 months	11
2 to 3 years	3
9 months to 3 years	7
4 to 8 years	12
9 to 20 years	4
more than 20 years	8
Age not given	4
Total	86

Case in an Infant.—The youngest case on record is that of Vacca† from an infant 20 days old, suffering from a resistant enteritis. In the second month "white segments" were seen in the dejecta and a month later, when alarming symptoms including extreme pupillary dilatation and stupor compelled the summoning of a physician, treatment resulted in the evacuation of a worm 105 mm. long, and the gradual restoration of the health of the infant. A cat had been introduced into the household six days after the birth of the infant and 12 before the onset of the intestinal disturbance. At necropsy the cat contained 31 specimens of *Dipylidium caninum*, and larval stages (cysticercoids) of the same tapeworm were detected in one of the fleas living on the cat.

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* Blanchard, R., Parasitisme du *Dipylidium caninum* dans l'espece humaine a propos d'un cas nouveau. Arch. de Parasit., xl (1907)pp. 439–471.

Encore un case de *Dipylidium caninum* a Paris. Arch. de Parasit., xvl (1914) pp. 438–448.

† Vacca, A., 1909. Elmintiasis da *Dipylidium caninum* (L.) in un bambino di 3 mesi d'età. Riv. di clin. pediat., Firenze, vii, pp. 739–745.

In one of the most striking cases a mother and four children in the same family were all infected and together harbored more than 200 well-developed specimens of this parasite.

Frequency.—The record of specimens thus far discovered is given in Table 11. It should be born in mind that the numbers are related to the frequency of the use of the microscope and to the accuracy of methods of clinical diagnosis rather than simply to the abundance or exact distribution of the parasites.

TABLE 11.—GEOGRAPHICAL DISTRIBUTION OF DIPYLIDIUM CANINUM IN MAN

COUNTRY	NUMBER OF CASES
France	6
Germany	16
Denmark	21
England	3
Scotland	2
Holland	1
Italy	2
Sicily	2
Norway	1
Sweden	2
Russia	3
Switzerland	7
Austria	10
Portugal	2
Cape Colony	1
German East Africa	1
Philippine Islands	1
United States	5
Venezuela	1

Rare in U. S.—That the parasite is rare in the human host in the United States may be inferred from the record of Judkins* who in 15,000 stool examinations in Texas found only two of this species. In 1903 Stiles reported the first case in the United States from a child of 16 months in Detroit, Michigan. The second case in America was published by Riley; it involved a boy of 11 years at Ithaca, New York. Such cases are certainly much more frequent than the records indicate.

Symptoms in Infants.—Even among infants the majority of cases show no special symptoms, the presence of characteristically shaped

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* Judkins, O. H., Some observations on intestinal parasites in Texas, based upon microscopic findings in 15,000 cases. Texas State J. Med., x (July, 1914), p. 126.

and colored segments causing discovery of the infection. In some instances, however, intestinal disturbances and even nervous complications, pain and emaciation have been noticed, as in infection with other intestinal helminthes.

FAMILY DAVAINEIDÆ Fuhrmann 1907
GENUS DAVAINEA Blanchard et Railliet 1891

Scolex spherical; rostellum prominent, sometimes retractile, armed with one or two rows of very small hammer-shaped hooks; suckers protruding, armed with several rows of minute hooks, often caducous. Genital pores unilateral or irregularly alternating. Uterus breaks up into capsules each enclosing one or several eggs. Development unknown. Many species parasitic in mammals and birds; only incidentally in man.

Davainea madagascariensis (Davaine 1869)

Synonyms.—*Taenia madagascariensis* Davaine 1869; *Taenia demerariensis* C. W. Daniels 1895.

This parasite is 250 to 400 mm. long with from 500 to 700 proglottids in the chain. The scolex, about 1 mm. in diameter, bears a thick retractile rostellum having five rows, often imperfect, of 110 hooks about 21 to 25μ long. The suckers are large, spherical and probably armed. The first proglottids are short and broad, later ones are square; the ripe segments measure 2 by 1.4 mm. and are shaped like apple seeds. The genital pores are unilateral with occasional transpositions. The eggs, in groups of two or three, are encased in heavy parenchyme capsules, 0.2 to 0.4 mm. in diameter, filling the entire ripe proglottid. The oncosphere is 8μ (or 15μ in Garrison's case) in diameter, with six slender nearly straight hooks from 4 to 5μ long, difficult to see.

This tapeworm grows very rapidly. The last hundred segments, which make up more than half the entire length of the worm, contain only eggs in capsules (see Fig. 373). The development is entirely unknown. Blanchard suspected that a cockroach was the intermediate host. The normal host is unknown, but this parasite has never been reported from any host except man. Nevertheless it is unlikely that so large a species could be overlooked in man; or if rare could maintain itself in the human host alone.

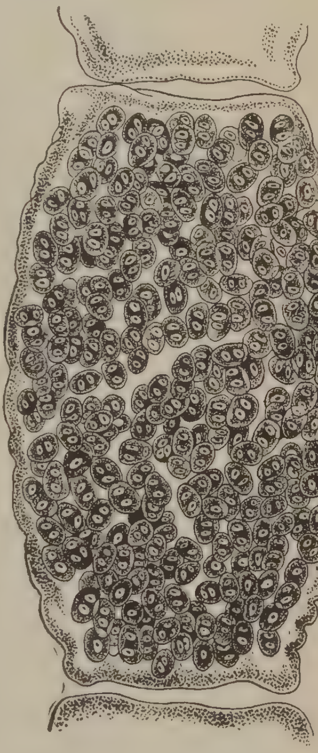

FIG. 373.—Ripe proglottid of *Davainea madagascariensis.* ×35. (After Braun.)

Incidence in Children.—Blanchard summarized eight cases from Siam, Madagascar, British Guiana, and the Antilles. The first six cases were all from infants and only two from adults. They all were reported from seaport towns and were apparently related to docks and ships. Garrison reported a case from Manila in 1911; the parasites were obtained at the necropsy of an adult male Filipino.

Davainea formosana, a related species reported by Akashi in 1916, was evacuated by an infant in Formosa. The normal host and manner of infecting the human species are both unknown. Even though a chance parasite of man, it may be significant in human pathology under circumstances.

FAMILY ANOPLOCEPHALIDÆ Kholodkovski 1902

The genus Bertiella Stiles and Hassall 1902 is a member of the sub-family Anoplocephalinae, which includes parasites of both mammals and birds. Among about 20 species, one is reported from the chimpanzee and a second as a common parasite of the orang-utan. A single specimen of the latter, *Bertiella satyri* (R. Blanchard 1891), was taken from an infant of that region, by Dr. Barbeau of the hospital laboratory at Port Louis on the island of Mauritius. By virtue of the normal host this record is of great interest.

ORDER BOTHRIOCEPHALOIDEA Braun 1903

These are polyzoic cestodes with two elongated sucking grooves (bothria) on the scolex, which is unarmed. They have a separate uterine pore which opens on the ventral surface of the proglottid. The common sexual pore lies on the same or opposite surface or at the margin. Since eggs are discharged constantly, no organs of the proglottid disappear during growth. The eggs are covered as in Trematoda. The oncosphere is not formed when the eggs are laid. The larval forms are worm-like and without caudal bladder. These cestodes are parasitic mostly in lower vertebrates; a few species are found in man.

FAMILY DIPHYLLOBOTHRIIDÆ Lühe 1910

GENUS DIPHYLLOBOTHRIUM Cobbold 1858

Synonyms.—Dibothriocephalus Lühe 1899.

Scolex much elongated, simple; sucking grooves weak, unarmed. Genital orifices all on ventral surface, not far apart, in anterior region of proglottid. Genital organs single; uterus coiled near center of proglottid in a characteristic rosette. Larval form, plerocercoid, found in muscles and body cavity of fishes.

Diphyllobothrium latum (Linnaeus 1758)

Synonyms.—*Bothriocephalus latus* Bremser 1819; *Taenia vulgaris* and *T. lata* Linnaeus 1758; *Dibothrium latum* Diesing 1850; *Dibothriocephalus latus* Lühe 1899.

The broad or fish tapeworm of man is from two to nine meters in length, rarely reaching 20 meters, with from 3000 to 4200 proglottids. It is grayish-yellow in life. The head is an elongated oval, measuring 2 to 5 mm. by 0.7 to 1 mm.; two longitudinal grooves, or bothria, traverse the dorsal and ventral surfaces which by torsion of the neck appear to be lateral. The first proglottids are indistinct, and broader than long (Fig. 345); near the center of the chain they are much larger and show a dark lobed area in the center of each; near the end the proglottids grow narrower and finally irregular; when detached and discharged in groups they are difficult to recognize. The genital cloaca opens on a papilla in the mid-ventral line near the anterior margin; the uterine pore or tocostome, also ventral and median, lies a little farther back, and from it eggs are discharged continuously after the full development of the dark area, which is the egg-filled uterine rosette. The eggs are operculate, brown, and contain a developed embryo some days before they are evacuated in the feces. Magath's* study was made on eggs from macerated proglottids and establishes the range of length between 55 and 76μ, and of width between 41 and 56μ, with an average size of 64 by 47μ. He rightly emphasizes in diagnosis the importance of form (Fig. 375), which includes the lid and a small nodule at the opposite pole.

Hosts.—The adult is parasitic in the small intestine of man and the cat; the larva (plerocercoid) in the muscles and among the viscera of many fish.

The structure of the fish tapeworm can be easily made out by examining Figs. 374, 376. It differs in many particulars from the Taenias, most strikingly perhaps in the convoluted uterus with a uterine pore. The accumulation of eggs in the folds of the uterus produces the thickened central area and the lobed, dark brown rosette, which are conspicuous external features of the older proglottids in the chain. The uterine pore permits the escape of the ova, and the terminal proglottids in the chain have lost nearly all of them. In consequence these proglottids are small and shriveled.

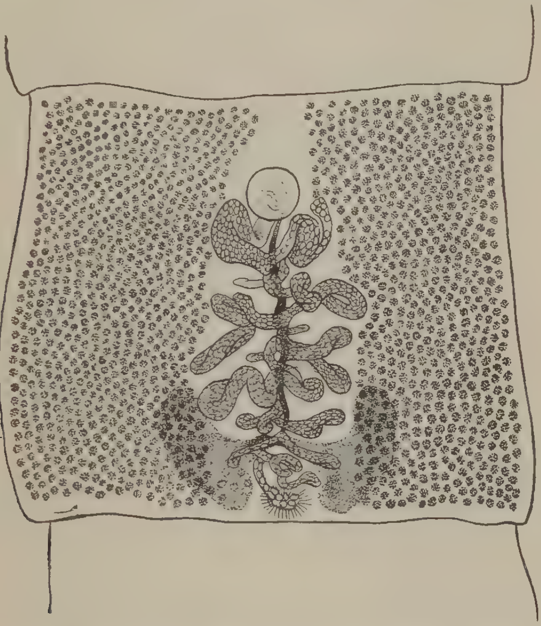

FIG. 374.—Sexually mature proglottid of *Diphyllobothrium latum.* ×15. (After Braun.)

Life Cycle.—The development of this species involves two intermediate hosts. The eggs evacuated in the feces remain unchanged until they are brought by chance into water. Then the cover is loosened and the ciliated embryo escapes. Within it has been developed a hexacanth embryo, and after this is completed it is ready for the first intermediate host, which is a small crustacean (*Cyclops strenuus* and *Diaptomus gracilis* in Switzerland according to Janicki and Rosen). When the ciliated free-swimming stage is ingested by such a crustacean, the embryo becomes free and penetrates into the body cavity of the host. Here it is transformed into a long sausage-shaped larva known as a procercoid. This possesses a spherical pedicel bearing the embryonic hooks and a dermal coating of fine spines. After two or three weeks growth in the crustacean, the larva increases from 24μ to 0.5 or 0.6 mm. in length. If then the infected Cyclops is swallowed by a young fish (trout, perch) the larva is set free and passes through the alimentary wall to the muscles and viscera. This migration is slow and while in young fish the larva may reach the liver in six days, in older fish from 15 to 30 days are required. Increase in size and development of its suckers completes the plerocercoid stage. This is the form infective for the human host. M. Braun first discovered in the Baltic provinces these plerocercoids in a long series of European food fish, including the pike, burbot, perch, salmon, trout, white fish, grayling and others. In such fish these larvæ attain a length of from 10 to 20 mm. with a breadth of 2 to 3 mm. and can read-

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* Magath, T. B., The Eggs of *Diphyllobothrium latum.* J. A. M. A., lxxiii (July 12, 1919), pp. 85–87.

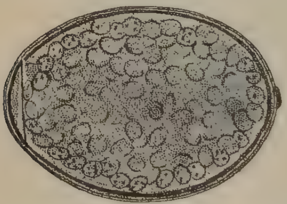

FIG. 375.

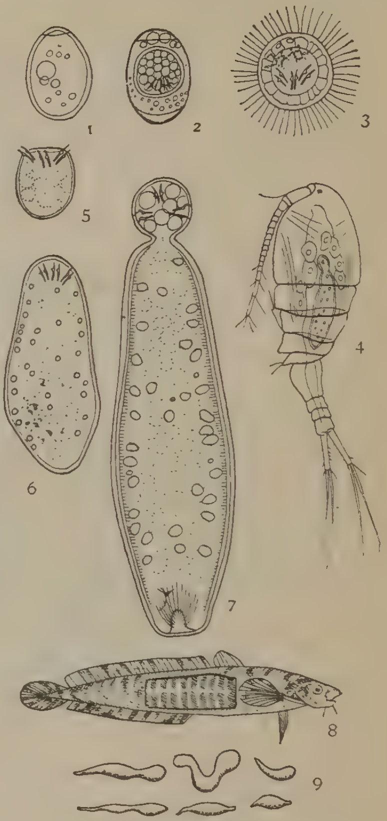

FIG. 376.

FIG. 375.—Egg of *Diphyllobothrium latum*. Note lid and nodule at opposite pole. × 500. (After Magath.)

FIG. 376.—Life cycle of *Diphyllobothrium latum*. 1, egg, embryo not yet developed, from intestine of man; 2, hexacanth ciliated embryo within egg shell after three to four weeks in outer world; 3, ciliated embryo free containing oncosphere. It lives only a few hours in water but 4, if ingested by a *Cyclops strennuus* it loses its ciliated envelope and becomes 5, in the body cavity of the copepod, where by growth; 6, 7, in 20 days it attains a maximum size the procercoid larva; when the cyclops 8, with the procercoid larvæ is eaten by certain fish they become in a few weeks, 9, plerocercoid larvæ which can infect man, dog and cat. (After Brumpt.)

ily be distinguished among the viscera by their chalky white color. Living larva were obtained from smoked, salted and frozen (Fig. 377) fish as well as in the roe of the pike, which is salted and eaten raw as caviar. These observations of Braun were verified in Switzerland by Zschokke and in Scandinavia and Japan. Various experiments determined positively the relation of the larvæ to the human tapeworm. Once introduced into the human intestine the worm develops very rapidly, growing 6 to 9 cm. per day in some cases. Eggs appear in the feces of the human host from 24 to 30 days after the ingestion of the living larvæ.

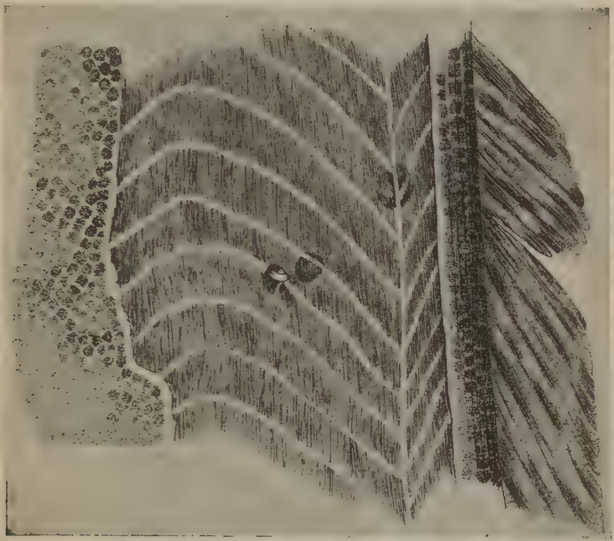

FIG. 377.—*Diphyllobothrium latum.* Portion of body wall of fish (*Loto vulgaris*) with plerocercoid *in situ.* Magnified. (After Braun.)

Variations.—Anomalies are not as common as in Taenia although some occur. Slender specimens and giants are recorded; prismatic and fenestrated varieties have been described. The commonest malformation, duplication of pores and sex organs in a single proglottid, is seen in any specimen carefully examined. One variety (*D. cristatum*) possesses a longitudinal ridge on each flat surface of the scolex.

Distribution.—The adult is cosmopolitan in fish eating regions and especially abundant in those that are near water bodies, affording a plentiful supply of fresh fish. These regions are along the Scandinavian, Finnish, and other Baltic coasts; even as far inland as Moscow and Warsaw, in Switzerland around Lake Geneva, where in most recent years it is growing rare; in Italy about the Italian lakes; in Russian Turkestan; in Japan, and finally in Madagascar and around Lake N'gami in central Africa.

Formerly in this country *D. latum* was regarded as a rare curiosity and present only in immigrants from infested European districts.

The first case was studied by Dr. Joseph Leidy in 1879 and more than 100 cases are on record up to 1922; 65 of them in Minnesota were listed by Nickerson* and several in the Upper Peninsula of Michigan by Warthin.† Most of these records concern adults who despite, in some cases, long residence in this country *might* have brought the parasite from Europe.

Incidence in Children.—Nickerson‡ was the first to furnish evidence of infection with the broad tapeworm originating without question in the United States. Among cases reported from Minnesota he recorded one at Ely, Minnesota, in a boy 2½ years old who had never been outside the state and who had not eaten imported fish. Several years later he published data on the case of a woman who had never been out of Minnesota, except for a visit once in North Dakota, and who had not eaten imported fish. The next records, given by Warthin, mention several Finns in Upper Michigan who had been brought to this country as suckling infants and had experienced no trouble until after 10 to 16 or more years of life here. One of his cases concerns a girl of five in that region who had never been out of the country. Later Becker gave an account of this parasite from a Russian Jewish boy, aged 11 years and a native of Chicago. Again in Minnesota, Riley reported this cestode from a Minneapolis boy of eight and a Chippewa Indian child on the reservation. Later accounts add two such cases from Chicago and one from Fort Wayne, Indiana. Very likely others also have been observed and perhaps put in print. At least 10 clear cases of native infection are on record and several others are probably native also. Of Minnesota, Riley writes that this species is the most common large human cestode in certain districts of the state. Warthin had expressed similar views about the mining region of Upper Michigan in 1912. Evidence is rapidly accumulating of the existence of the broad tapeworm in still other parts of the country.

It is important to avoid possible confusion. Warthin records this cestode from a gray fox in northern Michigan, and Hall and Wigdor described *Diphyllobothrium americanum* from a dog in Detroit. The fox parasite may be the same species and also some at least of the cases from man. Ward has collected adult bothriocephalid tapeworms from bears in the northwestern United States and in Alaska, and the larval stages of these cestodes in salmon in those regions. These parasites were undoubtedly endemic. The species from man may be the same but in very few human cases has the parasite been examined with care. Nickerson properly emphasizes the importance of utilizing parasitologists as consultants in order to secure exact data and eliminate confusion from the records of parasitic diseases.

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* Nickerson, W. S., 1911. Some Data Concerning *Dibothriocephalus latus* in America with Report of a Second Case of Infection Acquired in the United States. Science, xxxiii (Feb. 17, 1911), p. 270.

† Warthin, A. S., 1912. Report of the Occurrence of the Fish Tapeworm (*Dibothriocephalus latus*) in Michigan. Public Health, Michigan, vii (Jan. to Mar., 1912), p. 78.

‡ Nickerson, W. S., 1906. The Broad Tapeworm in Minnesota, with the Report of a Case of Infection Acquired in the State. Jour. Amer. Med. Assn., xlvi (Mar., 1906), pp. 711–713.

Source of Infection.—The mode of infection in Europe, discovered by Braun and verified by other students, has already been outlined and something similar might be expected here. Almost every case listed in North America gives a history of the eating of fish, often smoked, salted or raw, after the customs prevalent in the Old World. Warthin found plerocercoids in burbot roe (Fig. 378). He records one case in a child born in the United States in a family who often ate burbot roe uncooked. It is necessary to emphasize the need of caution regarding these cases. In a review on Medical Helminthology on Cestodes Leiper recently wrote: "As Nickerson had frequently found the larva of *B. latus* in fish caught in the Great Lakes, it seemed probable that its occurrence [i.e. the adult tapeworm in the United States] had been overlooked." Now Nickerson not only did not make such a statement but he distinctly endeavored to guard against such an interpretation. He wrote: "Larvæ of Dibothriocephalus do occur in American fishes. I have obtained them from fish caught in the Great Lakes *but without feeding experiments it is impossible to determine the species of Dibothriocephalus and the probability is in favor of such larvæ being of some species other* than *latus*, the parasite of man." The error, into which Leiper and others fell, has been widely disseminated by the citation of Singer and Kapelowitz who first made it, until today it is quoted in many articles and in various general texts. Certain it is that the Great Lakes and some other northern waters contain fish infected with bothriocephalid larvæ that grow to adult form in man and probably also in the dog and cat. The infection is therefore likely to spread. At present endemic foci are known to be located in Michigan, Minnesota, Indiana and Illinois. Probably North Dakota, Wisconsin and Ohio are involved. There is no direct danger from carriers of the adult parasite although they constantly spread the infection unless precautions are taken. As Lyon* states, "For the last six years many thousands of eggs must have entered the sewage system of South Bend, very soon to reach the St. Joseph River and a short time later Lake Michigan. In both river and lake hatching larvæ must have been able to parasitize various fishes." General public health demands that this danger be reduced if it cannot be entirely eliminated. The consumption of uncooked or imperfectly cooked fish should be carefully avoided.

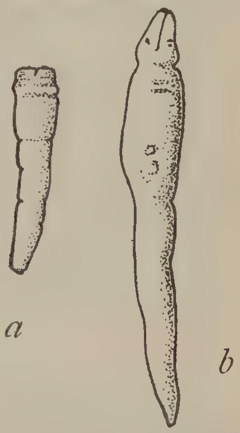

FIG. 378.—Plerocercoid of *Diphyllobothrium latum.* *a*, head invaginated; *b*, extended. Magnified. (After Braun.)

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* Lyon, M. W., Jr., Infection by broad tapeworm, *Diphyllobothrium latum.* J.A.M.A., lxxiv (March 6, 1920), p. 655.

Toxicity.—The broad tapeworm is one of the most serious of human parasites by reason of the marked anemia associated with its presence, and designated bothriocephalid anemia. Huber states that the symptom-complex is characteristically that of primary pernicious anemia with a mortality of 16 per cent. unless the worm is removed. Usually the expulsion of the parasite is accompanied within a few hours by a marked improvement progressing rapidly to complete recovery, but in some cases, even after the parasite has been dislodged, a progressive and fatal anemia develops. Several American case histories emphasize the fact that the classic symptoms were wanting whereas others describe the anemia as serious. Tallquist extracted three toxic substances from ripe proglottids, a proteolytic ferment, a hemagglutinin and a hemolysin. According to his researches, these toxins are not eliminated from the cestode during life but only as the worm or parts of it are killed and macerated. Then the absorption by the host induces the anemia. In 70 per cent of Schaumann's cases in Finland the anemia was definitely associated with the presence of disintegrating parasites. This has been clearly shown in other cases.* If the complete worm is not removed, the trouble will recur when the chain has grown out again, *i.e.*, in about three months. The species seems to be difficult to expel completely and recurrence is frequent. Most of the numerous record of great longevity attributed to this parasite are involved in the objection that reinfection is not excluded.

RELATED SPECIES

Diphyllobothrium cordatum (R. Leuckart 1863) is an allied species reported once from man in Greenland where it is common in the dog, seal and walrus. It is evidently sporadic in the human host and may easily recur as such, especially in children.

Diphyllobothrium parvum (Stephens 1908) was described from fragments evacuated by a Syrian resident in Australia. A like form was reported from this country by Magath. According to Zschokke this type is only a very small, stunted or crippled variety of *D. latum.*

Diphyllobothrium americanum Hall and Wigdor 1916 a fox parasite is discussed above. For reasons given there it is likely to infect children since the young host is more susceptilble than the adult.

Diphyllobothrium mansoni (Cobbold 1882)†

Synonyms.—*Ligula mansoni* Cobbold 1882; *Bothriocephalus liguloides* Leuckart 1886; *Bothriocephalus mansoni* R. Blanchard 1888; *Sparganum baxteri* Sambon 1907; *Sparganum raillieti* v. Ratz 1912.

The adult parasite from the dog has been experimentally bred and studied by recent Japanese investigators. Yamata in 1916 fed larva to a dog and raised a large bothriocephalid; Yoshida confirmed this experimentally in 1917. The worm was 2.5 meters long. The eggs differ distinctly from those of *Diphyllobothrium latum*, being darker brown and measuring, according to Yoshida, from 62 by 37μ to 77 by 43μ, which is about the same size though the form is different.

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* R. L. Haden, The Cause of Bothriocephalus Anemia. Am. J. Med. Sci., xvi (1923), p. 338.

† The correct generic name of this species is uncertain.

The larva, which is found in man as well as in numerous other hosts is 80 to 600 mm. long by 1 to 12 mm. broad, very contractile and variable. The body is flat, striated or folded but without proglottids. The anterior end is enlarged and rounded with two faintly indicated bothria. In the necropsy of a Chinese, Manson first found a dozen specimens below the peritoneum and one free in the body cavity. Other cases have been reported from China, Indo-China, and Japan, recently what purports to be the same species has been found in a leg abscess of a Masai in East Africa and in a native of British Guiana. Cases are also reported from Australia and Texas. The determination of species from the larvæ alone without feeding experiments is uncertain since the larvæ are undifferentiated in structure and highly variable in size and shape. Hence such cases cannot be definitely assigned to any particular species. The larval form is characteristic of the group of bothriocephalid tapeworms and not of any single species. Both larvæ and adult of these tapeworms utilize a wide range of hosts, including such cosmopolitan species as dog, cat, and rat, so that wide dissemination is easy and the menace to man is evident.

Ocular Sparganosis.—It is the larval form, designated formerly as Sparganum, which is found in the human host and is the cause of serious troubles by virtue of the location it often selects in the human body.

In the East many of the cases are from children and especially in Annam take the form known as ocular sparganosis. In Motais' case,* a boy, aged 11, who was born and lived in Hue, Annam, had noted occasional redness of the eyes for a year. A small swelling appeared on the upper left lid, and grew slowly to the size of a bean. The tumor was deep seated, mobile and easily removed. The capsule consisted of dense vascular connective tissue and was filled with fluid in which floated the larval sparganum. The surgeon recorded the frequent occurrence of similar parasites in pigs in Annam. In ocular sparganosis the larval parasite may occur either under the bulbar conjunctiva or in the orbit. In some cases it is alive, in others dead or even degenerating. Diagnosis may be made by the presence of edema if accompanied by a tumor in one lid. The larvæ secured by incision of the mass are very much smaller than those originally described by Manson. He found the original specimens beneath the peritoneum.

Sparganum proliferum (Ijima 1905)

Synonyms.—*Plerocercoides prolifer* Ijima 1905; *Plerocercus prolifer* Ijima 1905; *Gatesius prolifer* Stiles 1908.

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* Motais, F., 1921. Ocular Sparganosis. Ann. d'oculistique, clviii, p. 329.

This is a larval form of which the adult is unknown. The length is from 1 to 12 mm., the breadth about 2.5 mm. The head is very active, without bothria, but with rudimentary apical suckers. The larva is capable of reproducing by transverse division and of budding off supernumerary heads that later become independent individuals. It is found encysted in subdermal connective tissue. Cases have been reported from Japan by several observers and from Florida by Stiles and Gates in 1907.

Cases in Man.—The first case was described by Ijima from Japan in 1904. The worms came from little cysts estimated to number more than 10,000 in the left thigh alone. This enormous infection was undoubtedly due to the ability of the larva to multiply asexually. Efforts to raise the adult by feeding the larva to pigs, dogs and cats were unsuccessful. The case from Florida was similar; the host, a fisherman, had apparently suffered from the infection for 25 years, and during that period the trouble had increased from a few pimples to many enclosing larva similar to the Japanese form. These two widely separated cases agree in location near the ocean and in the fish diet of the hosts; so we may conjecture that the normal adult host was an edible fish, cosmopolitan in its range.

It is of importance in this paper to note the extremely long duration of the trouble. Such an infection acquired even in early childhood would last over into middle life, and the apparently indefinite power of multiplication makes the parasite a serious liability to the human host.

GENUS DIPLOGONOPORUS Lönnberg 1892

Synonym.—Krabbea R. Blanchard 1894.

Scolex with powerfully developed bothria. No neck. Genital organs identical with those of Diphyllobothrium, but double in each proglottid. Genital orifices in two series right and left of median line, located in two longitudinal grooves that divide ventral surface approximately into thirds.

Diplogonoporus grandis Lühe 1899

Synonym.—*Krabbea grandis* R. Blanchard, 1894. Bothriocephalus sp. Ijima and Kurimoto 1894.

Adult 10 meters in length and from 1.5 mm. broad near scolex to 25 mm. broad at posterior end. Proglottids very short and broad. Uterine coils few and wide, two in each proglottid. Eggs brown, thick-shelled, 48 to 50 by 63μ.

This parasite of seals and Cetacea has been found in man in Japan. The unknown larva doubtless came from some fish consumed uncooked.

A second species, *Diplogonoporus brauni*, has been reported twice from Roumania by Leon, in company with *Diphyllobothrium latum.*

Braunia jassyensis Leon, which came from Roumania also, lacks external proglottid markings. It is probably only sporadically a human parasite and yet of unquestioned significance like the other Bothriocephalids.

NEMATHELMINTHES

The phylum Nemathelminthes or roundworms embraces three classes. The three classes have little in common except a certain similarity in external form and marked simplicity of structure. They are elongated and generally cylindrical with a uniform, rather monotonous external appearance. The three classes are the Nematoda or true roundworms, the Gordiacea or hair worms, and the Acanthocephala or proboscis roundworms. In general the Nematoda taper more or less toward one or both ends, and possess a smooth glistening colorless exterior. The Gordiacea are larger, more uniformly cylindrical with bluntly rounded ends and a faintly colored or particolored external layer. The Acanthocephala exhibit a roughened surface, sometimes with imperfect or irregular annulations, and approach the form of a carrot. The differences are sufficiently marked to separate specimens at sight. Only the Nematoda are of marked importance in human parasitology.

III. NEMATODA

These are elongated cylindrical worms, often filiform but at times more spindle shaped and regularly tapering from the central region towards one or both ends. The human parasites among these worms vary in size from less than a millimeter to nearly a meter in length. Contrary to conditions that obtain among trematodes and cestodes, among which there are no free-living species, nematodes are widely distributed as free-living forms in fresh water, in the ocean, in the earth, in slime, among decaying substances, and as parasites in the tissues of plants as well as in the most varied locations in animal hosts.

Description.—Externally the body is smooth but under the microscope appears faintly annulate; these lines are surface striations and do not indicate any internal division into segments. Around the anterior end are found papillæ, bristles, hooks, and lip-like outgrowths of irregular form. These are usually more or less definitely related to the mouth opening, which lies at the extreme anterior tip of the body and is sometimes provided with an oral capsule and a complex dental apparatus. Near the posterior end one finds modifications of somewhat similar type. They are, however, ordinarily in front of the tip of the body, and only rarely is the anal opening also exactly at the posterior end.

The sexes are easily distinguished externally, the male being smaller than the female and displaying a coiled or twisted posterior end, whereas the tail of the female is simple and usually straight with the axis of the body. The genital pore in the female lies in the midventral line and usually near the center of the body, although in some genera it is removed from that point almost to the anterior or posterior tip of the body. In the male the reproductive organs empty into the terminal section of the alimentary canal, and the sex cells are expelled through the anus. In the posterior ventral region the male carries a series of papillæ, varying greatly in different species in number, size, form and arrangement: These are generally used as diagnostic characters. The male has sometimes also lateral expansions of the cuticula in the form of long folds (alæ) without fleshy supports, or a shorter somewhat bell-shaped bursa composed of two lateral, often continuous, cuticular outgrowths with fleshy rays; both types are clasping organs. In a few genera a series of surface ridges in the male, or a pre-anal sucker in both sexes serves the same purpose. These structures are prominent and distinguish readily between the groups of alate, bursate and nonbursate nematodes, a classification used by some writers.

On the surface of the body one can usually see very distinctly, even in alcoholic specimens, two narrow bands; these are designated the lateral lines, lateral fields or lateral areas and extend the length of the body; midway between them lie the somewhat similar, but less conspicuous, dorsal and ventral lines. Owing to uniformity in external appearance and difficulties in technique these worms are not easily differentiated.

Larger nematodes are opaque, but the smaller forms are transparent and the internal structure may readily be seen. The alimentary canal extends directly through the body. It has a buccal cavity, often with complex cutting apparatus, a heavy muscular esophagus (Fig. 379) terminated in many forms by a bulb, a thin-walled intestine, and a short narrow rectum. The heavy muscular body wall encloses a spacious unlined body cavity in which lie the tubular reproductive organs, filling most of the space with their coils. In the female the system is double and the fine ends of the tubes are the two ovaries; the larger uterus, usually of the bicornuate type, is conspicuous by reason of the mass of eggs or developing embryos that it contains. Near the pore one finds a special unpaired apparatus, the ovijector, often used in species descriptions. The male system has only a single filiform testis terminating in a larger vesicula seminalis and a ductus ejaculatorius. Near the anus and often projecting from it, are conspicuous chitinous spicules that vary in number, form and relative position; they are much used as specific characters.

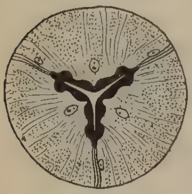

FIG. 379.—Cross section of esophagus of hookworm *Ancylostoma duodenale*. (After Looss.) Magnified.

Life Cycle.—The development of nematodes is sometimes direct and simple, and in other instances complicated by the introduction of an intermediate host or of some special condition to provide for the transfer from one individual to another of the host species. The transfer may be brought about incidentally by the introduction of the eggs or embryos with polluted food or water. It may also take place through the activity of the larva in boring its way into the tissues of the host. Or a blood sucking insect may inject the parasite into the host from which the insect is abstracting nourishment. In such cases as this, well represented by the life history of the blood inhabiting filariæ, the parasite never comes in contact with the outside world. An equally highly specialized condition is illustrated by the trichina. Here the young larvæ are encysted in the same host that shelters the adult and these encysted forms secure further opportunity for development only when the flesh in which they are encysted is eaten by a susceptible host and they are set free to achieve sexual maturity in the intestine. The females here produce migrating larvæ that are carried to distant parts of the body in which they become encysted. Recent investigations have revealed in some species unsuspected migrations which emphasize the dangerous character of those forms whose larvæ undertake migrations through the human tissues of considerable length and complexity before they attain the location and stage in which they are fitted to enter the final period of the life cycle, that of sexual maturity.

Importance.—The roundworms contribute more species to the list of human parasites than do the trematodes or cestodes. They furnish also a larger number of children's parasites, although there are only a few species which are exclusively or primarily characteristic of the child. Most of the species are readily recognized, and the treatment of cases in which they occur has been subject to careful consideration ever since the earliest days of medical practice. Species are constantly being introduced into new territory, and infection establishes itself often with unexpected readiness. Furthermore, among the smaller forms, increased care in observation is constantly disclosing the presence of previously unknown forms or demonstrating the greater frequency of species regarded as rare or occasional. The clinical importance of many species has been ignored or entirely overlooked.

Anticoagulin.—Some parasitic nematodes, especially the Strongyles, which have a buccal capsule fitted to lacerate the intestinal mucosa, secrete substances that inhibit the coagulation of the blood. These substances, which apparently are not identical in different species, show a relationship to hirudin and snake venom. They cause the persistent oozing of blood from wounds inflicted in the mucosa by the armature of the buccal capsule. Evidently such minute hemorrhages are of marked etiologic significance. This condition was first discovered by Loeb and Smith for the dog hookworm and has been since demonstrated for a long series of other forms.*

FAMILY ANGUILLULIDÆ *Oerley* 1882

The family of the Anguillulidæ contains a few parasites almost indistinguishable from the many free-living species that characterize it. The worms are of small size, transparent, delicate and tapering toward both ends. The mouth is armed with two teeth or a chitinous stiletto. The inflated esophagus carries one or two bulbs at the posterior end. Double symmetrical uteri containing only a few very large ova, short reflexed ovaries, and a vulva near the center of the body, characterize the female. The male possesses two equal spicules, with or without an accessory piece. The ova develop rapidly and some species are ovoviviparous.

GENUS RHABDITIS *Dujardin* 1845

No teeth in buccal cavity. Two bulbs on esophagus, posterior one dentate and behind nerve ring. Spicules two, short, with accessory piece.

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*Schwartz, B. Effects of Secretions of Certain Parasitic Nematodes on Coagulation of Blood. Jour. Parasit., vii (Mar., 1921), pp. 144–151.

Rhabditis niellyi (R. Blanchard 1885)

Synonym.—*Anguillula leptodera?* Nielly 1882; *Leptodera niellyi* R. Bl. 1885.

Known only in the larval form. Discovered by Nielly in 1882 in a boy living near Brest in France and never away from the region. The worms were found in papules of a dermal eruption and were attributed to the lad's habit of drinking from brooks; more probably they were larvæ of some filaria. Dermatoses caused by larval nematodes are recorded from various animals in Europe and somewhat similar cases are reported in man by several observers.

Rhabditis hominis Kobayashi 1914

The female is from 1.5 to 2 mm. long and 0.12 mm. broad. The body is cylindrical, the anterior end tapering gradually, the posterior end more abruptly. There are four labial palpi. The esophagus has four muscular regions. The anterior region, broad, 0.17 to 0.2 mm. long; the anterior bulbus about at the center; the posterior region, much narrower but slightly longer than the anterior, and the posterior bulbus, slightly smaller than the anterior. The excretory orifice is at the level of the posterior bulb. The anterior uterus is longer than the posterior in young specimens with from 10 to 15 eggs and in adult females filled with embryos already hatched out.

The adult male is from 0.9 to 1.2 mm. long and from 0.03 to 0.05 mm. broad. It has two sickle-shaped spicules approximately equal, from 35 to 41μ long. A rod-shaped gubernaculum is also present. There are six pairs of stalked papillæ, in three groups: two pre-anal, two postanal, and the others nearly adanal.

No Pathologic Significance.—In the feces of primary school pupils examined in Japan, this species occurred in great abundance in all stages of development in the same material. The percentage of infection among 1100 boys and girls between 10 and 14 years of age was less than 2 per cent. Only larval and adult forms occurred in the feces, no eggs being found. Re-examination two months later of 4 out of 17 infected children demonstrated that all were free from the parasite, which accordingly is to be regarded as temporary or accidental. The presence of large numbers of these nematodes was not accompanied by any evidence of general or local disease.* The species is probably not a true parasite but introduced by chance contamination.

Heterodera radicicola (Greef, 1872)

Synonyms.—*Oxyuris incognita* Kofoid and White 1919.

In 1919 Kofoid† reported a previously unknown nematode ovum in the stools of soldiers in Texas. Later reports of a similar character concerned other parts of the United States and other countries as well. Such findings came mostly from extensive stool examinations in hookworm campaigns. The egg, which was clearly differentiated from that of any known human intestinal parasite, was the basis for the name *Oxyuris incognita* since its asymmetry suggested a relation to the family

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* Kobayashi, H., On a new species of rhabditoid worms found in the human intestines. J. Parasit., vi (March, 1920), p. 148.

† Kofoid, C. A., New nematode infection of man. J.A.M.A., lxxii (Feb. 22, 1919), p. 567.

Oxyuridæ, to which the hypothetical adult was assigned even though all attempts to secure it by the administration of various anthelmintics had failed. The size of the egg, and in addition, the two highly refractive, hyaline blue-green globules, usually flattened asymmetrically at the poles of the egg, were sufficient to demonstrate its unique position among human helminth ova. The egg measured on the average 95 by 40μ but ranged in size from 68 to 133μ by 33 to 43μ, dimensions greater than those of the ovum of any previously known human intestinal worm.

From the sporadic appearance of these ova in the stools and their frequency during the summer especially, when vegetable salads are prominent in the diet, Sandground* was led to experiment with the root nematode, *Heterodera radicicola*, which is both widely distributed and extremely common. He observed that the ova of this species pass through the human alimentary canal apparently uninjured and that they are in appearance in every respect indistinguishable from the eggs of the supposed *Oxyuris incognita*. In one case the larva was also positively identified as that of *H. radicicola*. The suggested identity of the eggs of the two forms furnished an adequate explanation of the sporadic occurrence of the ova in the original and later findings, as well as of other anomalies in various cases. Even though not as yet especially connected with findings in children, these ova may easily turn up at any time in such hosts. The history of this species is a particularly vivid illustration of the complications that are to be met with and must be guarded against in this field.

FAMILY ANGIOSTOMIDÆ Blanchard 1895

The family of the Angiostomidæ (Rhabdonemidæ) includes small forms much like the Anguillulidæ; but they manifest metagenesis in that a free diecious, rhabditiform generation alternates with a parasitic, hermaphroditic or parthenogenetic generation which is filariform.

GENUS STRONGYLOIDES Grassi 1879

Parasitic generation with simple unarmed mouth, having four lips; cylindrical esophagus very long, of strongyloid type. Free generation with oral cavity and esophagus with two bulbs (rhabditoid type), anterior bulb unarmed and fusiform, posterior bulb spherical and dentate. Male with two small similar spicules.

The parasitic generation occurs in the intestine of man and various other mammals; the free generation lives in earth and decaying materials. One species is a serious human parasite.

Strongyloides stercoralis (Bavay 1876)

Synonyms.—*Anguillula intestinalis* and *A. stercoralis* Bavay 1876 nec *A. intestinalis* Ehrenb. 1838; *Leptodera intestinalis* and *L. stercoralis* Cobbold 1879; *Str. intestinalis* Grassi 1883; *Rhabdonema intestinale* R. Bl. 1886; *Rh. strongyloides* Leuckart 1883.

Parasitic generation (Bavay's *A. intestinalis*).—These are female only, parthenogenetic; from 2.1 to 2.2 mm. long, from 60 to 70 μ wide; the body tapering anteriorly, and the posterior tip short, blunt end conical. The mouth has four inconspicuous lips. The esophagus is cylindrical, uniform, one-fourth the length of the body. The vulva is transverse in the posterior third of the body. The uterus is bicornuate, containing from 5 to 9 ova measuring 50 to 59 by 30 to 34μ (rarely up to 65 by 39μ), often joined in strings of two or three.

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* Sandground, J. H., "*Oxyuris incognita*" or *Heterodera radicicola*. Jour. Parasit., x (Dec., 1923), pp. 92–94.

Free generation (Bavay's *A. stercoralis*).—Males and females are present. The body is slender, tapering toward both ends. The oral papillae are indistinct. The esophagus is only 0.16 mm. long, rhabditiform, with two bulbs. The male is from 0.75 to 1 mm. long and from 35 to 66μ thick, with short recurved caudal end, and two conspicuous, conical spicules, often protruding, 38μ long. The female is from 1 to 1.4 mm. long and from 50 to 75μ wide, with long, slender, pointed tail. The vulva is behind the center of the body, on the right side. The uterus is double. The thin-shelled eggs, 70 by 45 μ, are often hatched within the body of the mother. The embryos at first have a pointed tail, a bulbous esophagus and chitinous teeth, but soon change to the filariform type.

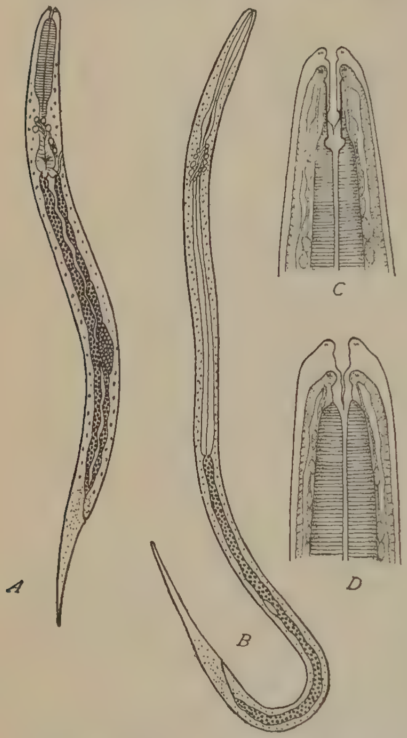

Fig. 380.—Larvæ of *a*, *Strongyloides stercoralis* and *b*, *Ancylostoma duodenale* ×225; heads of *c*, *Astercoralis* and *d*, *A. duodenale*, after first moult within old larval skin, ×700. (After Looss.)

Life Cycle.—As Askanazy first showed, the parasitic generation lives not in the lumen but in the wall of the intestine, and the ova are deposited ordinarily in the glands of the intestinal wall. These ova hatch before being discharged from the host; hence one ordinarily finds larvæ in the feces and only rarely eggs of this parasite. These larvæ (Fig. 380) are difficult to differentiate from those of the hookworm unless care is exercised. A differential diagnosis is often important. The strongyloid larvæ, 200 to 300μ long by 14 to 16μ broad, may undergo one molt and become filariform larvæ (strongyloid type); in this form they are infective and if introduced into the human alimentary canal are transformed into parthenogenetic females. Such is the method of direct development.

However, after the first molt the larvæ may grow greatly, and give rise to adult males and females. From the fertilized ova produced by these worms, there come rhabditoid larvæ which molt and become infective filariform larvæ. This is the indirect development or heterogeny. The view that temperature or the character of the surrounding medium influenced the production of the two types of larvæ was shown by Brumpt* to be incorrect.

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* Brumpt, E., Recherches sur le determinisme des sexes et de l'evolution des Anguillules parasites (Strongyloides). C. R. soc. biol., lxxxv (June, 1921), p. 149.

In both types of development the infecting larvæ gain access to the human host by penetrating the skin; or if ingested they bore into the mucosa. From here they are taken up by the circulation and carried to the lungs. They emerge into the air sacs, and ascending the trachea they enter and travel down the alimentary canal to become adult in the intestine in from 10 to 15 days. Larvæ of a new generation first appear in the stools in 17 days or less.

Distribution.—This worm was first discovered in 1876 by Dr. Normand during the micro-examination of stools of soldiers returned from Cochin China, who were affected with acute dysentery. It occurs rarely in Europe (in Italy, France, Germany, Belgium, Holland, and probably more widely); in tropical and subtropical regions it is usually common, being obtained in from 20 to 35 per cent. of cases examined. In the southern United States it is reported by Stiles and Garrison in 0.23 per cent. of cases from government hospitals, and in Georgia by Willets from 0.8 per cent. among recent admissions and from 17 per cent. of old cases. It occurs, though not so frequently much farther north, but thus far no exact or extensive records are at hand.

Importance in Children.—This parasite plays an active part in producing recurrent dysentery and serious complications. The invasion of the skin by the larvæ gives rise to a typical "miner's itch." The parasite is said to occur in the intestines or in the stools of persons of every race and age. Its frequency increases apparently with advancing years; Darling found the maximum percentage at Panama in patients of more than 50 years of age. Practically all data available are derived from examinations of adults, and in most instances from inmates of state and government hospitals. One record concerns children exclusively. In French Guinea a commission* in 1914–1916 examined stools of 154 children from 5 to 15 years of age and obtained Stongyloides in 10 cases; in one instance the larvæ were present in large numbers. The age at which the human host acquires this parasite is unknown as is also its length of life. Apparently the infection is cumulative. A study of these relations is evidently of great importance.

These worms are difficult to expel. At the Mayo Clinic seven cases have been treated for long periods with many anthelmintics, but without more than temporary effects.

FAMILY GNATHOSTOMIDÆ Blanchard 1895

The family of the Gnathostomidæ is characterized by a mouth with two lips and numerous chitinous plates like scales on the body or at least the anterior region. The species **Gnathostoma spinigerum** (R. Owen 1836) is a common parasite of dogs and cats in Siam, the Malay States and part of China. It occurs occasionally as an erratic parasite in man, causing a "creeping disease." The human parasite is not sexually mature and may be in the migrating stage. Another species, *G. hispidum* has also been reported recently.

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* Clapier, N., Notes sur le parasitisme intestinal par les nématodes dans la zone frontière du Liberia et de la Guinée. Bull. soc. path. exot., Paris, x (1917), pp. 560–563.

SUBORDER FILARIOIDEA Weinland 1858

The suborder of the Filarioidea includes very long and slender nematodes having no lips but usually a few small circumoral papillæ. The esophagus is simple and slender without a bulb. The female is usually ovoviviparous; the vulva far anterior; the ovary double. The male has a single spicule, or two unequal spicules; the posterior region is coiled in a close spiral with or without caudal alæ.

FAMILY FILARIIDÆ Claus 1885

Body very slender, greatly elongated. Head, straight, pointed, with two lateromedian and four submedian papillæ, and sometimes also small lips. Esophagus long, slender, and lacks bulbous enlargements. Male with coiled posterior region and either one spicule or two unequal ones. Female with double ovary, vulva in anterior region, persistent in adult. Mostly ovoviviparous.

The family includes a wide range of parasites of uniform external appearance and complex life histories. The larvæ to which the general name of Microfilaria is applied occur in the circulating blood and are transmitted to new hosts by some biting insect, in which they remain and undergo developmental changes. The adult forms inhabit connective tissues, serous cavities and lymphatic spaces. While the filariæ are important from the standpoint of disease in adults, they are less significant for children.

The single genus Filaria of earlier texts has necessarily been split up into a considerable number of new genera.

Into this group has been thrown any slender, elongate nematode that lacked distinctive structural features. Many of these still remain, almost unknown in fact, to encumber the family. As some have been studied, they have been recognized as distinct genera or transferred to some other family of nematodes. The doubtful forms are still left under the original genus Filaria. The immature stages are grouped under the general term Agamofilaria. The blood-inhabiting larvæ are very uniform in appearance and were the source of much confusion until Fülleborn's precise studies furnished a basis for differential diagnosis. Many such imperfectly described larvæ still remains doubtful and the relations between larvæ and adults have been definitely determined only in a few cases. The clinical importance of the larvæ calls for a brief account of methods for observing and differentiating them.

Technique.—When the blood is centrifuged, the microfilariæ are concentrated in the serum and may be preserved by adding 5 per cent. formalin, or if glacial acetic acid and gentian violet are also added they are stained at the same time. Blood smears are usually employed to detect them, and a thick smear dried rapidly is preferable to the thin smear advised for malarial organisms. Distilled water may be used to extract the hemoglobin, and immersion in absolute alcohol for five minutes serves to fix the preparation. Dark-field illumination is advantageous. Fülleborn recommends staining by the Romanowsky-Giemsa method.

The microfilariæ are transparent and also long and slender, being from 250 to 500μ in length and from 3 to 6μ in transverse diameter. The so-called sheath is of first importance. It is absent in some forms, and when present is easily overlooked on account of its delicacy. From the uterine development this sheath is regarded by some as the greatly distended vitelline membrane; other investigators regard it as the skin of the first molt. Within it the worm moves actively to and fro without changing location. The highly refractile, glass-clear cuticula of the larva can easily be seen, and within it an irregular mass of nuclei, arranged in areas and marking out certain "spots" used by various writers in diagnostic descriptions. Listed in order from the head backward these are (1) the nerve ring, (2) the so-called excretory cell and excretory pore (Manson's "V" spot), (3) the genital cell, and (4) the anal vesicle (Manson's tail spot). The relative positions of these four spots serve to characterize the different a species, as in Table 12, taken from Fülleborn.

TABLE 12.—RELATIVE POSITION OF DIAGNOSTIC POINTS IN COMMON BLOOD-INHABITING MICROFILARIÆ

Embryos	Sheath	Nerve ring	Excretory pore	Excretory cell	Genital cell	Anal pore	Last caudal cell	Actual length in μ
M. nocturna	+	19.6	29.6	30.6	70.6	82.4	95.1	162–291
diurna	+	21.6	31.6	36.6	68.6	81.9	at end	152–246
volvulus	0	24.2	*	....	69.5	†	95.6	297.5
perstans	0	21.4	....	38.5	*	79.1	at end	198.9

All measurements except the last column are percentages of total length.

* Not conspicuous. † About like the first two.

The form of the posterior end and the arrangement of the nuclei in it, as well as the form taken in blood smears, aid specific determination. Nearly all of these features may be modified by shrinkage, and in the extreme case very radically; hence perfected technique is essential if reliance is to be placed on results.

Periodicity of Microfilariæ.—The periodicity manifested by some microfilariæ in the circulating blood was first noted by Manson in 1879. One type which he named *F. nocturna* appeared in the peripheral blood late in the afternoon, increased to a maximum about midnight and vanished by 8 or 9 a.m. Later he designated another species *F. diurna*, that reversed these conditions, being first seen about 9 a.m., reaching a maximum at 1 p.m. and disappearing by 10 p.m. Despite individual variations and changes due to altered routine of the host, the periodic movement is generally constant though certain so-called "varieties" of *F. nocturna* and other species manifest no periodicity at all. The cause of the differences in periodicity is unknown. Manson observed that if the host spent the night at work but slept during the day, *F. nocturna* altered its periodicity correspondingly, but *F. diurna* could not be made to change its habits by such means. The microfilariæ live months, and apparently even years, in the circulating blood and may increase in size during that period.

Life Cycle.—In the normal life cycle these microfilariæ are transferred to a new host by a biting insect such as a fly or a mosquito. After being drawn into the insect's stomach with a mass of blood, the nematode deserts the sheath, if one be present, and boring through the gut wall, makes its way into the thoracic muscles, or less often the Malpighian vesicles. In this place the worm becomes much shorter and thicker ("sausage shaped") and enters an inactive stage. At the close of this growth period, the worm deserts its resting place and migrates through the body cavity into the labium. In the act of biting the mosquito turns the labium back against the surface of the skin, whereupon the young worms bore their way out and into the new host. It appears thus that the transfer is an active migration and not a passive inoculation. The subsequent changes consist only of growth to sexual maturity during the course of wanderings about in the connective or lymphatic tissue of the new host. Minor differences in detail constitute the individual features of the various species and will be noted in appropriate places later.

GENUS FILARIA O. F. Müller 1787

Mouth minute, no lips. Vulva always near anterior end. Spicules of male very unlike. Four pre-anal papillæ; post-anal papillæ variable. (This genus contains many poorly described forms and is constantly being revised.)

Filaria bancrofti Cobbold 1887

Synonyms.—[Embryos in blood stream] *F. sanguinis hominis* Lewis 1872; *F. sang. hom. aegyptiaca* Sonsino 1874; *F. sang. hom. nocturna* Manson 1891; *F. nocturna* Manson 1891; *Microfilaria nocturna* Shipley and Fearnsides 1906; *F. taniguchii* Penel 1905; *F. philippinensis* Ashburn and Craig 1906.

The body is elongated, white (when preserved, brown like a horsehair), opaque, very delicate, with a tendency to coil. The cuticula is not striated. There are two rows of oral papillæ. The male is from 35 to 40 mm. long, and from 0.1 to 0.12 mm. broad. The posterior region is coiled, the tip of the tail slightly recurved. There are eight peri-anal papillæ; the spicules are from 0.2 to 0.6 mm. long. The female is from 75 to 95 mm. long, and from 0.21 to 0.28 mm. broad, with the vulva from 0.72 to 1.27 mm. from the anterior tip, and the anus 0.282 mm. from the end of the tail. The embryos are from 0.127 to 0.2 mm. long by 8 to 10μ broad, enveloped in a delicate sheath.

Characteristics.—Demarquay first described the microfilariæ as early as 1863 and Bancroft the adult worms in 1876. But both were confused with other species and discrepancies in the descriptions and measurements of various authors are due to this confusion. The adults of both sexes curl up in inextricable masses in the lymph glands. The entire internal space of the female is filled with thin-walled uterine tubes containing ova and embryos in every stage of development.

The embryos in freshly drawn blood are in constant motion, twisting and coiling, but never exhibiting a true progressive movement. The delicate sheath in which each embryo is enclosed cannot be distinguished save as an apparent flagellum following the tail for 0.3 to 0.4 mm. When the movement of the body is reversed, this disappears at the tail and reappears on the head. A minute spine may be seen at the tip of the head, which is protruded rapidly at times in a peculiar "pouting" movement. Bancroft and Manson conjectured almost simultaneously that the mosquito might serve as a carrier, but Manson was the first to observe the changes that take place. The mosquito stage lasts from 12 to 18 days through some larvæ remain in the muscles of the mosquito even up to 50 days. Though the range is greater than usual, not all species of mosquito are available as intermediate hosts; some 10 or 12 species serve as such in different regions.

Distribution.—The parasite is distributed all around the world in the tropical and subtropical belt. It has been reported casually from various places in the United States. Most of these cases are without doubt imported but a few are endemic. In Charleston, South Carolina, from which extensive series of cases have been reported, the parasite is well established and 20 per cent. of 400 examined were infected.* *Culex fatigans* is the transmitting agent. One apparently endemic case† has been reported from Boston and in this instance elephantiasis was also present.

Incidence in Children.—In one set of examinations from Egypt near Cairo the incidence in children up to 19 years was 23 per cent. Another locality disclosed 25 children infected out of 315 examined; in five other adjacent districts, in the Loocho Islands, 13 per cent. of the children carried microfilariæ and 0.58 per cent. had elephantiasis. But in central Africa, in an infested region, only one child, a girl of four years, was infected among 122 children examined. In this connection comment was made on the great rarity of infantile filariasis. In a heavily infected district of Porto Rico this infection was present in patients of all ages from 5 to 50 years. Incipient elephantiasis is recorded for a girl of 14 in Alexandria, Egypt.

In French Guiana filariasis is wide-spread. It is exceptional in infants, the youngest infected being four years old, but from 20 to 25 per cent. of those examined between 10 and 15 years of age were infected. In Georgetown, British Guiana, in 1921, microfilariæ were obtained in the peripheral blood of a child only 14 months old, and three infected children were less than two years old. Among 200 children below 16 years, 12 per cent. were infected with microfilariæ and 60 per cent. had enlarged lymph glands. Indeed 2.6 per cent. of children under 16 suffered from elephantiasis, and the proportion of the population afflicted with this disease was higher in Georgetown than in any other city in the world. The comatose form of filariasis occurred in Porto Rico among children from 5 to 10 years of age. In a summary of 142 filarial cases recorded in eastern North America, Lyon* cites only a few cases in patients 15 years of age or less: a colored girl from Antigua, only a few months on the continent; a white girl, aged seven, who had lived in Florida and later in New Jersey, and several patients in Charleston, S. C., the youngest of whom was six years old.

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* Francis, E., Filariasis in Southern United States. U. S. Hyg. Lab. Bull., cxvii (June, 1919), 36 pp.

† Shattuck, G. C., Filariasis apparently contracted in Boston. Boston M. and S. J., clxxxix (July 26, 1923), p. 142.

In patients who became pregnant, the embryos were not detected in the child's blood or in the mother's milk. In Japan, however, Kawakami† reports a case of typical filarial fever in a girl only 60 days old, who was born in the endemic area. Frequent attacks thereafter were noted. During each attack erysipeloid of the skin appeared on both lower extremities. No error in diagnosis of typical elephantiasis lesions is likely in this case.

Pathology.—The presence of embryos in the circulating blood is evidence of the present or past parasitism of the adult in some part of the lymph system. The duration of life for the adult is certainly several years, and the embryos live at least as long. Leukocytosis with an increase of eosinophils is noted early as the effect of the presence of the young forms. More serious changes are attributed to the influence of the adults. It is held that they occlude large lymphatics and produce lymph stasis with resulting dilatation of the lymphatics. More probably the toxic metabolic products of the parasites evoke inflammatory changes and thickening of vascular walls. According to Manson, parasitism of *F. bancrofti* results in lymphangitis, varicose inguinal and axillary lymph glands, lymph scrotum, orchitis, chyluria, and various forms of elephantiasis. While elephantiasis doubtless has various causes, and while many cases of *F. bancrofti* do not manifest it, yet some causal relation probably exists: the degree of infection or its duration may be important. As many as 40 or 50 million embryos, without apparent effects have been estimated in the circulating blood of a single man.

Treatment.—*Prophylaxis.*—The destruction of mosquitoes and their breeding places, as well as protection of the individual against mosquito bites, are factors in a rational prophylaxis. An infected human host is an evident menace to any community in which susceptible mosquitoes occur, and *Culex fatigans* is common over considerable areas in the United States. The infected area in Charlestown probably owes its infection to the introduction from the West Indies or Africa of slaves carrying the disease. Oil of citronella, applied locally, is a popular preventive against insect bites.

Drugs.—There is no widely accepted treatment by which the parent filariæ, and with them the microfilariæ, can be destroyed. Tartar emetic, neosalvarsan and potassium picrate have been used with some success.

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* Lyon, M. W., Jr., Filariasis. J.A.M.A., lxviii (Jan. 13, 1917), p. 118.

† Kawakami, Zen., Report on Filariasis. Japan M. World, ii (Sept. 15, 1922), p. 252.

Symptomatic.—Varicose glands and vessels, unless causing great discomfort, are usually left alone. In severe cases of elephantoid fever, the swollen part may be pricked to allow exudation of the collecting lymph. In chyluria, atoxyl, arsenobenzol, and neosalvarsan exercise a beneficial effect in intravenous injections. In elephantiasis, the prognosis as to complete cure is not hopeful. However, general hygiene, avoidance of violent exercise, massage, and tight bandaging will often prevent growth. Surgical removal of elephantoid tissue, especially in the scrotum, can usually be accomplished successfully. Castellani reports cures in a few months from the injection of fibrolysin into the elephantoid tissue. However, surgical treatment affords the only real relief in elephantiasis.

OTHER SPECIES OF FILARIA IN MAN

Filaria conjunctivæ Addario 1885 has been found as a human parasite half a dozen times in small cysts in connective tissue, once in the eyelid; the cases were reported from southern and eastern Europe and India. Though it appears to be only an occasional parasite of man, no other host has been demonstrated for it as yet.

Filaria ozzardi Manson 1897 occurs abundantly in the West Indies and on the northern shore of South America, affecting in some places from 25 to 30 per cent. of the entire population. Thus far no pathologic effects have been recognized from its presence.

Filaria tucumana Biglieri and Araoz 1917 from the northern provinces of Argentina and known only in the larval form, is a frequent species, not well known but of evident importance.

Filaria hominis oris Leidy 1850 was "obtained from the mouth of a child." The case is isolated; very likely the specimen was accidentally introduced and should not be regarded as a usual human parasite. It has been provisionally identified as a Mermis (q.v.).

Agamofilaria georgiana Stiles 1907 was an immature form of which 18 specimens were obtained from an adult negress at Darien, Georgia. It must be regarded as accidental or erratic. It may, however, recur in the human host and, children are most likely to become infected with such stray parasites.

Dirofilaria magalhaesi R. Blanchard 1895 was discovered at a necropsy in Rio de Janeiro. Two adult parasites were taken from the left cardiac ventricle of a boy. The species is tough and wiry unlike the soft forms living in connective and glandular tissues. In many ways it resembles closely *D. immitis* of the dog, first described by Joseph Leidy of Philadelphia in 1856, and recorded often since then from the dog but never from the human host. The Brazilian form is probably only an accidental parasite of man, but its normal host is not known.

GENUS LOA *Stiles* 1905

Cuticula covered with numerous hemispherical bosses. Caudal papillæ of male are few in number but large.

Loa loa (Guyot 1778)

Synonyms.—*Filaria oculi* Gervais and van Beneden 1859; *Dracunculus oculi* Diesing 1861; *Dracunculus loa* Cobbold 1864; *F. loa* Aitken 1866; *F. diurna* Manson 1891.

The body is pale and translucent; the cuticula is thick, covered save on the first and last fifths of the body with small bosses. The head is conical, truncated, with six small papillæ on each side near the base of the conical region. The male is from 25 to 33 mm. long, and from 0.3 to 0.45 mm. broad. The tail tapers, is rounded and slightly curved ventrad; there are three rounded, stalked pre-anal and two smaller postanal papillæ on each side. There are two unequal spicules, 0.11 and 0.18 mm. long. The female is from 60 to 65 mm. long, and 0.5 mm. broad. Cuticular bosses extend nearly to the anterior and posterior ends. The vulva is located 2.5 mm. from anterior end. Eggs in utero measure 30 to 35 by 20 to 25μ. For embryos see table, page 1021.

Distribution.—First recorded in 1770, this species commanded wide attention as the "eye worm" in spite of its rarity. In 1906 was published an analytical synopsis* of 100 recorded cases in North America; since then many more have been studied.

The parasite lives by preference in subcutaneous connective tissue and carries out constant and extensive migrations about the body. It is present often in large and unsuspected numbers but becomes visible only occasionally. When it appears in the subcutaneous tissue around the eye it becomes conspicuous and is often extracted by a simple operation. Its movements in other parts remain unnoticed except for occasional fugitive tumefactions, known as "calabar swellings," which are thought to be due to periodic discharge of waste products or of embryos by wandering worms.

The parasite is at home in the country around the Gulf of Guinea and inland therefrom irregularly to central Africa. It was introduced into the western continent with the slave trade. Later cases are due to the return of missionaries, travelers and traders from infested regions. The worm lives a long time in the human host, cases of infection having been observed from 5 to 10 or 12 years after removal from an endemic region. Apparently development is slow.

Intermediate Host.—The microfilaria, which has a short sheath and a periodicity that gave it the name of *Microfilaria diurna*, but which is often modified by irregular hours on the part of the host, is taken up by the mangrove fly, *Chrysops dimidiatus* and *Ch. silaceus*. In this insect its development is rapid.

Incidence.—In villages in which this parasite occurs, almost all adults harbor it and blood examinations reveal 20 to 25 per cent. to be carriers of the microfilariæ. On the other hand, children, who are apparently even more subject to the bites of the fly, do not often show embryos in the blood. In some series of examinations positive findings reached 13 in 210 children examined; while in others these embryos were not found even once. In hospital operations in Kamerun for intramuscular abscesses attributed to filarial disease, the youngest patient was a girl of 14 years. The parasite is often associated in a single host with *Filaria perstans* and *Onchocerca volvulus*, microfilariæ of all three species being noted at the same time in the blood. The few cases first recorded from the West Indies in 1768 and 1795 include two of children five and eight years old; and Arrachart noted that in Santo Domingo young negroes were often attacked by this eye worm. The missionaries in Africa report that the school work of native children is interrupted by periodic visits of this parasite to the eye.

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* Ward, H. B., Studies on human parasites in North America. I. *Filaria loa*, J. Infect. Dis., iii (March 2, 1906), p. 37.

GENUS ACANTHOCHEILONEMA Cobbold 1870

Cuticula smooth or delicately striated longitudinally. Esophagus of two distinct regions, provided at distal end with two short lateral appendices. Male with coiled posterior end and two unequal spicules. Female with vulva in esophageal region; viviparous.

Acanthocheilonema perstans (Manson 1891)

Synonyms.—*Filaria sanguinis hominis minor* Manson 1891; *F. ozzardi* var. *truncata* Manson 1897; *F. perstans* Manson 1891.

The body is cylindrical; there is a cervical constriction behind the head. The male is from 40 to 45 mm. long and from 60 to 80μ broad. The four pairs of preanal papillæ and one pair of postanal are all very small and obscure. The female is from 70 to 80 mm. long and 0.12 mm. broad, with the vulva 0.6 mm. from the anterior end. The embryos are without a sheath, with an obtusely truncate tail; they are very small, extremely active and changeable, and measure from 100 to 200μ in length, and from 4 to 7μ in breadth.

Incidence.—The embryos were originally discovered by Manson in the blood of Congo negroes and some years later in the blood of natives of British Guiana. These microfilariæ do not manifest any periodicity. Although they develop in certain mosquitos the life history has not been worked out. Despite their earlier association with that disease they have no relation to sleeping sickness. The adult filariæ occur in connective tissue among the viscera and especially in the mesentery. The frequency of this species ranges from 30 per cent. of natives examined in Cameroon to 50 or even 85 per cent. in Congo territory. In general it is more common than *M. loa*.

In 210 examinations of children in the Congo-Cameroon district, Ringenbach and Guyomarch* found *M. perstans* in 56, *M. loa* in five, and both together in eight other cases.

GENUS ONCHOCERCA Diesing 1841

Cuticula thick, striated, with annular thickenings, or ribs, interrupted along lateral areas. Caudal papillæ of male often asymmetrical and variable, four paranal papillæ regularly present. Spicules unequal; longer pointed, shorter with enlarged or hooked end. Vulva near anterior end; two uteri. Viviparous.

Onchocerca volvulus R. Leuckart, 1893

The male is from 30 to 40 mm. long and 0.2 mm. broad at the center, tapering strongly toward both ends. There are no oral papillæ. The tail is coiled spirally and flattened ventrally. The cloaca is 70μ from the tip of the tail. The larger spicule is from 0.17 to 0.2 mm., the smaller only 0.07 to 0.08 mm. long. The female is 300 mm. long or more, 0.33 mm. broad at the center, tapering to fine pointed ends. The vulva is located from 0.5 to 0.7 mm. from anterior end. The walls of the uteri have dark spiral stripes.

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* Ringenbach, J. and Guyomarch, La Filariose dans les régions de la nouvelle frontière Congo-Cameron. Observations sur la transmission de *Microfilaria diurna* et de *Microfilaria perstans*. Bull. soc. path. exot., vii (July, 1914), pp. 619–626.

Pathology.—This long-known species is apparently a specific human parasite and confined to tropical West Africa between Sierra Leone and the mouth of the Congo. It produces large subdermal painless tumors, usually on the trunk, rarely on the head. The worm grows very slowly; Brumpt saw cases in patients of advanced age who, he was assured, had carried these modules since infancy. These tumors do not ulcerate. Dubois found that 15 to 20 per cent. of children were infected. The life cycle has not been worked out.

Incidence.—Larvæ of *O. volvulus* are found only rarely if ever in the blood, but according to recent investigations they occur in numbers in the skin. Such larvæ were discovered in many cases in which no tumors could be palpated; thus among 50 healthy men selected at random at Accra, the larvæ were demonstrated in the skin of 17, i.e. 34 per cent. In three necropsies larvæ were found in widely separated areas of the skin, though none could be demonstrated in the mucous membrane or in any organs, and no adult Onchocercæ were found in any part of the body.

Onchocerca caecutiens Brumpt 1919

The mouth is unarmed. The male measures 24 to 42 mm. long, by 0.15 to 0.19 mm. broad. There are no cuticular ribs. The caudal papillæ are asymmetrical, three adanal on the right, five on the left. The spicules are curved, 211 and 77μ long. The female is 500 mm. long and 0.3 mm. broad, with the vulva 0.8 mm. from the anterior end.

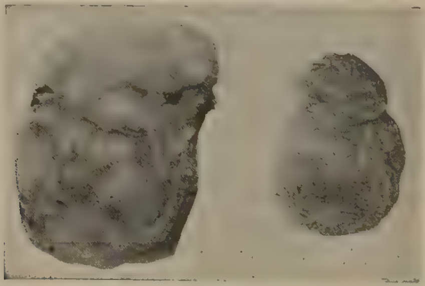

Fig. 381.—Cysts of *Onchocerca caecutiens*, from beneath the scalp of child; smaller, freed from superficial membranes shows coils of worm. Natural size, original figure. (Material by courtesy of Dr. Pacheco Luna.)

The embryo is without a sheath; it is 250μ long by 8 to 10μ broad. These embryos are never detected in the peripheral blood. The transmitting agent is doubtless a biting insect and some of the Simuliidæ are under suspicion, but the life history is still unknown.

Pathology.—This species, which is structurally much like *O. volvulus,* is found in a narrow territory on the west coast of Guatemala and in Mexico in altitudes between 600 and 1200 meters. It occasions subcutaneous, sebaceous tumors, (Fig. 381) found on the head in 99 per cent. of all cases; when located in the periosteum, the parasite may produce cranial perforations simulating trephining. In some infected zones the disease affects 97 per cent. of the population. It is a definite malady, known as coastal erysipelas, accompanied in some cases by an affection of the eyes that may proceed even to blindness and at times by auditory troubles. Extirpation of the tumors brings almost immediate relief.

The parasite lived seven years in one recorded case, but it apparently develops with unusual rapidity as tumors have been observed in persons who had lived only three months in the endemic zone, and one infant but 2 months old had a well-developed tumor.

Incidence in Children.—Children are commonly infected without regard to social conditions, age or sex. Infants at the breast may present the complete clinical syndrome.* In a male child of five months the disease developed fully in one month.

Fülleborn has described in detail the case of a boy of five from Mexico, affected with coast erysipelas. From the age of three this boy had manifested swelling of arms and face and also a bluish discoloration on one cheek. The condition was afebrile. A young brother, aged 3½ years, was similarly affected, and the father stated that nearly all white children and natives in the region were also affected. The territory lies on the Pacific Coast (Valle de Custipec) about 1000 meters above sea level. There were no optic troubles in this case, and Fülleborn notes that the majority of cases of oncocercosis he saw in Guatemala manifested none.

Treatment.—No treatment is effective except surgical removal of the tumors, involving only a simple operation the effects of which are immediate and most favorable. If the disease is not treated the sight is gravely impaired, and later treatment encounters permanent modifications. Fülleborn† believes that there is a relation between the improvement of vision and excision of the nodes.

FAMILY DRACUNCULIDÆ Leiper 1916

The family of the Dracunculidæ is characterized especially by the total disappearance of the vagina in the adult, the embryos being discharged by rupture of the gravid female. While the females grow to an enormous size the males are small and short-lived. The anus is closed in the adult.

GENUS DRACUNCULUS Kniphoff 1759

Vulva lacking in adult female. Larval stages at first free-living. Tissue parasites of reptiles and mammals.

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* Pacheco-Luna, R., Contribution to the study of onchocercosis. Am. J. Ophthalmology, Series 3, iv (March, 1921), p. 175.

† Fülleborn, Friedrich, The "Blinding Filaria" of Guatemala (*Onchocerca caecutiens* Brumpt 1919). J.A.M.A., lxxxiii (Oct. 18, 1924), p. 1269.

Dracunculus medinensis (Linnaeus 1758)

Synonyms.—*Gordius medinensis* L. 1758; *Filaria medinensis* Gmelin 1790; *F. dracunculus* Bremser 1819; *F. aethiopica* Valenciennes 1856; *Dracunculus persarum* Kaempfer 1694.

The female may be 1 m. long (ordinarily 60 to 90 cm.) and from 0.5 to 2 mm. broad. The body is cylindrical, white or yellowish brown. The mouth is small, with papillæ on the cephalic shield, which carries also near the margin six smaller papillæ. The alimentary canal is atrophied in the adult, and with other internal organs replaced by an enormously developed uterus which is crowded full of larval filariæ, from 0.5 to 0.75 mm. long and from 15 to 25 μ broad. The male is relatively small and not well known.

The guinea-worm, as it is popularly designated, is a common parasite of man and records of its presence go back into remote antiquity. The adult female occurs in ulcers in subdermal tissue. When such an ulcer has opened by a minute pore, a dash of cold water on the surface near it is followed by the protrusion of the tip of the worm and the exudation of a drop of milky fluid, which consists of a mass of active larvæ more advanced in development than the blood-inhabiting microfilariæ of other genera of filariæ. In a moist environment these larvæ may live even twenty days, swimming actively about without growth changes. Under favorable circumstances they enter aquatic organisms (Cyclops) and reach the body cavity in which they grow, and in from four to six weeks are ready for transfer. This is brought about by the ingestion of the Cyclops in surface water used for drinking. In the course of from 350 to 435 days, mature female worms have developed and are discharging young from ulcers in the new host. These ulcers are most common on the lower extremities but may be on other parts of the body.

Distribution.—This parasite is most abundant in central India and on the west coast of Africa. It occurs frequently also in Persia, Turkestan and Arabia. Introduced into the western hemisphere by the slave trade, it has disappeared from Curaçao and Surinam, where it was formerly endemic, and exists now only in a limited area in Brazil (Bahia). Occasional cases were reported from the United States but it never gained a footing here.

Incidence.—The mortality from the disease is low, but the local population is incapacitated for labor. While those of all races, ages and both sexes are infected equally readily, the disease limits greatly the activity of those in the most vigorous period of life and is of economic significance especially among laborers and soldiers.

Treatment.—The removal of the adult worm by direct surgical interference has proved a simple matter in the hands of medical missionaries located in infested regions. Émily, a medical missionary in Marchand, tried injecting the body of the guinea-worm, or tissue in which it is coiled, with a 1:1000 solution of mercuric chloride. This kills the worm and usually makes extraction easy after a few hours. Or the affected part may be bathed at frequent intervals for two or three weeks, until the guinea-worm has emptied its uterus. Then gentle pulling is likely to bring the worm forth, but if not its body is quickly absorbed by the tissues.

SUBORDER SPIRUROIDEA Railliet and Henry 1915

The Spiruroidea are long and slender, though not so extreme in these respects as the Filarioidea. They are easily distinguished from the latter by the esophagus which is differentiated into an anterior muscular and a posterior granular region. The male carries posterior lateral alæ which are long, narrow and without radiating fleshy ribs or supports. The species are numerous and important parasites, but only a few of them occur in man, probably purely adventitiously.

FAMILY SPIRURIDÆ Oerley 1885

GONGYLONEMA Molin 1857

The genus lives in the adult condition in burrows formed usually in the mucosa of the esophagus or the stomach. A species parasitic in the rat produces carcinomatous lesions. The species *Gongylonema pulchrum* Molin 1857 was removed by Covington from the lower lip of a 16 year old girl.* The worm (Fig. 382) migrated through the tissues from the lips to the fauces several times before its removal. This species is normally parasitic in the pig and has been bred experimentally in the croton bug as an intermediate host. One can readily infer that the infection of the human host was brought about by contaminated food. A second case, reported by Stiles as *G. scutatum*, involved a white girl, 13 years old, in Bushnell, Fla. Here also the parasite was taken from the lower lip. A third case, in which the species could not be determined, concerned a woman of 50 in Georgia. One case, assigned by G. Alessandrini to *G. subtile* concerns a youth of 18 in Rome, Italy. The worm emerged from the mouth. While rare, these cases all, with one exception, concern patients 13 to 18 years of age.

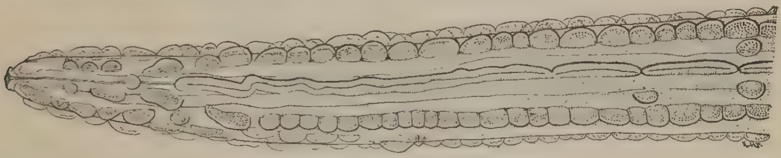

Fig. 382.—Anterior end of female Gongylonema pulchrum from human host. Original ×100.

GENUS HABRONEMA Diesing 1861

This genus which has recently attracted notice contains two species which in the adult stage are parasites in the stomach of the horse. Embryos of this worm while still enclosed in the egg shell are evacuated with the feces of the host, and are taken up normally by fly larvæ which develop in horse manure. The parasites undergo some changes within the fly, remaining in the insect during its transformation. They are deposited by the adult fly on exposed parts of the mucous membrane of the horse and produce there characteristic granulomata.

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* Ward, H. B., Gongylonema in the rôle of a human parasite. J. Parasitology, ii (March, 1916), p. 119.

"Bung Eye."—L. B. Bull* suggests that the invasion of the conjunctiva by larval Habronema may be responsible for some cases of "Bung Eye" common in Australia. He cites the case of a child who had on the under upper lid a characteristic granuloma and who five weeks before this had suffered from "Bung Eye." After a time the spaces occupied by the larvæ and also the larvæ themselves disappear, leaving only the granulomatous condition. This has been attributed hitherto to inflammatory edema produced in the loose tissue of the lids by the stings of poisonous insects.

PHYSALOPTERA Rudolphi 1819

In the genus are contained a large number of species with lacerating mouth parts that are serious intestinal parasites of the higher vertebrates. They occur usually attached to the wall of the stomach and produce chronic inflammation associated with adenomata of large size.

Physaloptera caucasica von Linstow 1902 was reported once from a man in the Caucasus.

Physaloptera mordens Leiper 1908 was observed in negroes in Transvaal, Uganda, and Portugese East Africa in numerous cases. It resembles a young Ascaris in appearance and confusion may readily occur. Both this and the preceding species are only accidental parasites of man.

FAMILY THELAZIIDÆ Railliet 1916

THELAZIA Bosc 1819

The genus contains species that inhabit the conjunctival sac of mammals and birds. They provoke ophthalmias in various domestic and wild mammals that are of economic significance.

Thelazia callipaeda Railliet and Henry 1910 is common in the eye of the dog in the far East, and what is probably the same species has been observed in the human eye in China. The intimate association of children with dogs makes infection in children more probable than in adults. However, cases thus far reported concern adults only. The living worms are pinkish and inhabit the lachrymal ducts, from which they often wander into the conjunctival sac and over the surface of the eye.

FAMILY DIOCTOPHYMIDÆ Raillet 1915

In the genus Dioctophyme (usually but wrongly referred to as Eustrongylus), one of the few species, *D. renale* (Goeze 1782), is a kidney parasite of many fish-eating mammals and is rarely seen in man. It is the giant of all nematodes, the female reaching a length of one meter with a diameter of from 5 to 12 mm. The fully developed parasite occupies the pelvis of the kidney or less often the body cavity.

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* Bull, L. B., Habronemic Conjunctivitis in Man Producing a "Bung Eye," Med. Jour. Australia, ii (Oct. 28, 1922), p. 499.

The unknown intermediate host has been conjectured to be a fish. Said to be not rare in dogs in Chicago and common in dogs in North Carolina.

FAMILY MERMITHIDÆ Braun 1883

The Mermithidæ have an obliquely striated cuticula and in the adult form neither mouth nor anus are functional. Externally they resemble the Filariidæ but are parasitic only in early life, the adult being free-living. The early stages are passed in insects, and chance introduction into the body results in their being reported as human parasites. Two probable cases were described by Leidy as *Filaria restiformis* and *F. hominis-oris* but assigned by Stiles to the genus Agamomermis. The second species is of especial import here since Leidy found the specimen in the collection of the Philadelphia Academy with the label "Obtained from the mouth of a child." He could give no further data. In 1881 Lockwood cited in detail three cases in which a white thread-worm, later identified as a Mermis, was detected in the core of an apple that some one was eating. The worms were parasites originally of some insect in the apple and might easily be taken into the mouth by accident. It seems probable that Leidy's case also belongs in the same class. Such occurrences are evidently most probable with children.

SUBORDER TRICHINELLOIDEA Hall 1916

These nematodes have an esophagus consisting of a capillary chitinous tube traversing a chain of single cells.

FAMILY TRICHINELLIDÆ Ward 1907

Delicate, transparent, much elongated body having two distinct regions: anterior slender part containing esophagus; posterior shorter and somewhat inflated portion with reproductive organs. Anus terminal. Male with single, simple, sheathed spicule, or none. Female with simple ovary; vulva at junction of two regions of body. (Among the genera are two which include the commonest and most feared of human parasites.)

GENUS TRICHURIS Roederer, 1761

Synonyms.—*Trichocephalus* Goeze 1782; *Mastigodes* Zeder 1803.

Anterior region very long and filiform; posterior region short, sharply marked off from anterior and much inflated. Male with spirally rolled-up posterior region: one spicule present with infundibuliform sheath. Female with posterior region slightly arcuate. Eggs ellipsoidal, with thick shell having transparent plug at each end. Parasitic in large intestine and cecum of mammals. Development without intermediate host but sometimes with migration through tissues before sexually mature.

Trichuris trichiura (Linnaeus 1771)

Synonyms.—*Ascaris trichiura* L. 1771; *Trichocephalus trichiura* Goeze 1782; *Trichocephalus hominis* Schrank 1788; *Trichocephalus dispar* Rudolphi 1801; *Mastigodes hominis* Zeder 1803.

The male is from 30 to 45 mm. long, with an extremely attenuated anterior region comprising three-fifths of the total length. The spicule is 2.5 mm. long, the sheath protractile and spinous. The female is from 35 to 50 mm. long, with an attenuated anterior region two-thirds of total length. The eggs are 51 to 53 μ long by 21 to 23 μ wide, brownish; they are deposited before cleavage begins.

Mode of Infection.—The whip worm is a common parasite of man, inhabiting usually the cecum and the appendix, less often the colon and rarely the small intestine; it lies with the anterior end threaded through the mucosa. The eggs when eliminated in fecal matter have not started cleavage and develop slowly in the outer world, the embryo not reaching full size for 6 to 12 months. Infection is brought about by the accidental swallowing of eggs with well-developed embryos. Grassi and Calandruccio infected themselves experimentally by swallowing such ripe eggs. The development is very rapid. Fülleborn* discovered that the young larvæ possess a protrusible oral stylet, but apparently do not carry out any migration to the liver and lung after the manner of Ascaris. They usually emerge from the shell in the large intestine and settle there. This is contrary to the views expressed by some other recent investigators and also contradicts the evidence afforded by the oral stylet.

Distribution.—The parasite is cosmopolitan in distribution, being naturally more abundant in warm climates. In Europe it varies from a frequency of 0.18 per cent. at necropsies in Petrograd to almost 100 per cent. in southern Italy. Brumpt sets recent figures for Paris as 30 per cent. for adults and 38 per cent. for children of 1 to 11 years. Balland gives 55 per cent. for adults in Paris. It seems to be growing rarer in recent years except for the period of the war. Usually only a few specimens occur in a single host but at times they are very numerous; Rudolphi reported more than 1000 in one case.

Symptoms.—The whipworm feeds on blood, which has been demonstrated in its intestine. The presence of the parasite produces an anemia which may be pernicious in degree, due to toxins as in other parasitic anemias, rather than merely to the blood extracted. To the whipworm has been attributed in the past an active rôle in the etiology of typhoid and cholera, but without reason. More recently it has been regarded as an etiologic factor in appendicitis. While apparently careful examinations by various parasitologists have rarely disclosed its presence the subject certainly has not been adequately investigated and deserves renewed study such as has very recently been devoted to the role of the pin-worm in appendicitis (q. v.).

Often the presence of the whipworm is not accompanied by any untoward symptoms, but at other times it apparently evokes severe digestive disturbances or nervous troubles. Thus Semon reported trichotillomania in a boy of six, persistent from the age of three and promptly corrected by removal of the worms.

Incidence in Children.—Among children it is reported as present in 43 per cent. of 160 examined in Denmark (Hansen). In the Philippines the findings of various investigators record a variation in incidence from 6 to 87 per cent. The analysis of cases of Crowell and Hammack (Phil. J. Sci., 8 B: 166; June 1913) apparently contradicts the frequent assertion that Trichuris is more prevalent in females and children than in males and adults. In the series of 500 cases, there were 120 cases of Trichuris in males, or 34 per cent., and 52 cases or 35 per cent. among females examined. In all, 15 per cent. of those under 15 years of age were infected and 40 per cent. of those over 15 years. In Columbia, Montoya holds Trichuris responsible for most chronic dysenteriform diarrhea among town children. In Manaos (Brazil) da Matta recorded it in 523 out of 883 children under 12 years of age he had examined during 12 years; this is 82. 3 per cent. of all cases. Moosbrügger in 1895 reported a fatal case in a boy of three with extreme anemia. In the child's intestine were found 442 male and 447 female whipworms; the immediate cause of death was croup. Da Matta* described two fatal cases from Brazil, in boys, aged four and eight years respectively; the whipworms were exclusively responsible for the conditions. In the first case 295 worms were found and in the second 120. The children manifested advanced anemia and edema, and various treatments were of no avail.

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* Fülleborn, F., Uber den "Mundstachel" der Trichotracheliden-Larven und Bemerkungen über die jüngsten Stadien von *Trichocephalus trichiurus*. Arch. Schiffs. u. Trop-Hyg., xxvii (Nov. 1923), pp. 421–425.

Treatment of Whipworms.—It is difficult to dislodge the whipworm, probably because of its firm attachment by the long slender "neck." The worms are located for the most part in the cecum. Not everything that passes the ileocecal valve enters the cecum. Anthelmintic drugs are partly absorbed and more or less diluted when they reach the ileocecal valve. Hall's experimental work indicates that the best treatment is the administration of small doses of anthelmintics over long periods of time, in order to insure their entrance into the cecum. Santonin has been used; oil of chenopodium, administered as for hookworm, is an effective remedy. In Columbia P. Berrio secured good results by giving to adults 30 to 40 gm. of fresh latex of *Ficus glabrata.*

Hepaticola hepatica (Bancroft 1893), a common parasite of the rat, has been detected in India as a human parasite in a liver abscess. It may occur elsewhere in children under poor sanitary conditions.

Infection with this species has been suggested as a means of exterminating rats, but the increased danger of infecting man incident to this method, makes it clearly undesirable.

GENUS TRICHINELLA Railliet 1895

Synonym.—*Trichina* Owen 1835.

Very small, slender, with regions of body not sharply set off. No spicule in male, but small lateral posterior appendages present. Female ovoviviparous; vulva at anterior fifth of the body. Only one species.

Trichinella spiralis (Owen 1835)

Synonym.—*Trichina spiralis* Owen 1835.

The male is from 1.4 to 1.6 mm. long, and 0.06 mm. broad. The fully developed larva measures 0.8 to 1.0 by 0.04 mm.; the cyst 0.4 by 0.25 mm.

The sexually mature parasite inhabits the small intestine of various mammals. Man, pig, rat, mouse, guinea pig and rabbit are easily infected; sheep, calf, and horse less readily, and cat, dog and badger with difficulty. Intestinal forms grow to maturity in birds but the embryos are expelled with the feces and never reach the muscles. Encysted larvæ were discovered in London by Peacock in 1828 and recognized as encapsulated entozoa by Paget in 1835. The case was described by the comparative anatomist, Richard Owen. These observations were soon confirmed in various countries by many workers. In the United States, Joseph Leidy announced the discovery in 1856 of similar worms in pork. The intestinal form was long regarded as the young, partly-grown stage of a Trichuris, or Strongylus. Feeding experiments by Leuckart, Virchow and Küchenmeister and the observations of Zenker on a maid who had died of apparent typhoid led ultimately to the elucidation of the life history. Isolated cases and epidemics of trichinosis, mostly in north Germany, demonstrated beyond question the serious rôle of the parasite.

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* Da Matta, Alfr., Considerations sur l'entero-trichocephalose et la trichocephalose appendiculaire. Bull. soc. path. exot., x (Dec. 12, 1917).

Life History.—When a piece of muscle containing living encysted larvæ is eaten by a suitable host, the worms are released by stomach digestion and pass into the small intestine. Two or three days suffice for the attainment of sexual maturity and soon after copulation the male dies. The gravid female bores into a villus and, lying with the vulva in a lymph vessel, discharges living young into the lymph stream. In about eight days these young reach striated muscle tissue. At birth they measure 0.09 to 0.11 mm. by 5 to 6μ and those found in intramuscular connective tissue from 0.12 to 0.16 mm. in length. The larva penetrates a muscle fiber, which undergoes granular and fatty degeneration, and the worm then rolls up in a loose spiral amid the remnants of the completely degenerated fiber. Connective tissue corpuscles and leukocytes produce about the worm a cyst of characteristic form, thickened at the poles and measuring about 0.4 by 0.25 mm. The formation of such a cyst requires several weeks. As the adult female lives some five to seven weeks and gives birth to from 800 to 2000 young, one finds in the muscle for a time all stages of development and encystment side by side. But soon the process is completed and the larvæ become quiescent.

Cysts.—Usually the formation of a calcareous layer or deposit about the cyst is noticed later. This gradually encroaches on the worm until ultimately the entire cyst is involved and becomes a mere calcareous nodule enclosing a remnant of the larva. Encysted trichinæ have been observed living 25 and even 31 years after the supposed period of infection, but more frequently all the larvæ have perished by calcareous or fatty degeneration. The death of the larvæ is regarded by some as a necessary preliminary to such degeneration.

Trichinosis.—The rat is usually regarded as the normal host of this parasite, and the method of transmission is clearly connected with the cannibalism prevalent in that species. The species was probably introduced into Europe from the East with the brown or Norway rat. Since pigs catch and eat rats eagerly, the general infection of swine was brought about, and the parasite is transmitted to man with improperly cooked pork products. The pig is regarded by some as the normal host since it is so well attuned to the disease.

Epidemics in the human host were formerly frequent in North Germany. In Saxony alone 30 epidemics were recorded from 1860 to 1879; they affected 1267 persons among whom 19 died. At Hedersleben, a town of only 2000 inhabitants, in one epidemic in 1865 a total of 337 persons were ill and 101 died. A campaign of education and the introduction of systematic meat inspection has reduced greatly in recent years the incidence from trichinosis. But in spite of the thorough organization of the inspection system at immense cost to the nation, security from trichinosis has not been attained, since the records of 20 years still show from 1881 to 1898 some 6329 cases and 318 deaths, more than one-third of which were due to meat inspected and passed as free. In the United States, Stiles has collected for 1860 to 1895 records of 900 cases, Ransom lists 1558 cases with 240 deaths between 1842 and 1914, but probably many more were not reported and indeed not recognized. I know of two cases that were diagnosed as atypical typhoid and rheumatism, respectively. A careful microscopic study of 505 cadavers by Williams revealed that 5.34 per cent. were infected with trichina; only two of these however, gave macroscopic evidence of the infection. These subjects came, however, largely from institutions. Osler's series of 1000 was representative but not handled so thoroughly.

Diagnosis.—The parasites are most abundant in the diaphragm and tongue, and in the intercostal and neck muscles. They occur at times in almost incredible abundance; Leuckart has calculated that some 30 to 40 millions were present in a single human host. It is customary to test the diagnosis of the disease by microscopic examination of a bit of muscle for the larvæ. This is easily taken from the anterior axillary fold of the pectoralis major in order to get the maximum number of parasites. The intercostals are better but more difficult to excise. Young trichinæ have been found in blood taken from the ear vein as late as 28 days after infection. The possible presence of other minute nematodes calls for great care in reaching a final decision. Cases of false trichinæ are well known in medical literature. The so-called "cell body" of the esophagus, which is very prominent in the narrower, anterior end of the young worm, is easily recognized in all stages of growth and in both sexes; it is of definite diagnostic value. Church suppers and family diarrhea in the country and in small towns should always suggest the possibility of infection with trichina.

Cases in Children.—Trichinosis is mild in children as a rule. Various German investigators attribute this to (1) weakness of the stomach juices and hence interference with the liberation of the encysted trichinae; (2) extrusion of large undigested pieces of meat with frequent bowel movements, and (3) shortness of the intestinal tract. In an epidemic in New York in which 10 Italians were affected and two died, Van Cott and Lintz reported that the four children, aged from 3½ to 12 years suffered only slightly from the disease and were the first to recover. Only one child, aged eight, suffered from marked prostration, but all symptoms had disappeared at the end of three weeks and recovery was complete. These authors suggest that children eat a much smaller quantity of the infected meat and hence ingest fewer parasites. Experimentally, the severity of the disease is in direct proportion to the number of parasites ingested. In these cases the trichinæ were never discovered in the feces in spite of repeated careful examinations. Furthermore, they were not detected in the circulating blood although a large quantity was tested; however, the larvæ were discovered in the spinal fluid and kept living in its for some days. One of the patients, who died of the disease, nursed an infant through her entire illness and the infant remained apparently perfectly well. No attempt was made to discover the larvæ either in the mother's milk or in the infant.

In an investigation of another epidemic, involving 14 persons, Salzer found trichinæ in large numbers in the milk of a nursing woman and also in a piece of excised mammary gland. He detected trichinæ in the blood in nine out of 14 cases, in the pus of a furuncle, and in a pleural exudate; they were abundant in the placenta but not present in the uterus. The urine was free from trichinæ in all cases, but the stools contained them always during the disease and in three cases after recovery. They were easily demonstrated by making the stools alkaline and letting them stand 12 to 24 hours. In 8 out of 14 cases trichinæ were readily obtained in the cerebrospinal fluid, and in a child of three, they were still in this fluid three months after clinical recovery. The feces were clay colored throughout the disease in every case, also later in the five cases that remained under observation. Other observers have reported larval trichinæ in the spinal fluid, but mostly without symptoms referable to the brain and cord.

Symptoms of Trichinosis.—Ordinarily the child has copious diarrhea, without fever, and recovers quickly. But in the rare case in which an older child partakes of large quantities of infected meat, the symptoms may be severe: Three stages are distinguished beginning, according to Ransom, with gastro-intestinal symptoms and in about a week followed by edema of the face, especially of the eyelids; the second stage follows in 9 or 10 days with intense muscular pains and disturbed function of the eye muscles, jaw muscles, and muscles of respiration. At about the sixth week the final, third period begins in which edema becomes general, followed by skin eruptions and scaling. The anemia is sometimes severe. If pneumonia does not supervene from the fourth to the sixth week, recovery usually sets in but strength returns slowly.

The disease frequently simulates typhoid or rheumatism. It has been confused with smallpox. Often it is not diagnosed at all and has been detected by chance in operations for goiter, etc.

In 1918 Meyer* described three cases in the same family, in girls of 12 and 6, and in a boy of 8, in which distinct meningeal symptoms were observed and in two of which trichinæ were found in the spina fluid. Meyer calls attention to the necessity of differentiating such early meningeal cases from poliomyelitis.

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* Meyer, J., Trichinosis. J.A.M.A., lxx (March 2, 1918), p. 588.

Eosinophilia is a constant accompaniment of trichinosis and results from a specific influence of the trichinæ, very likely through some toxin given off which stimulates the formation of the eosinophilic cells. In severe cases eosinophilia may be absent. It does not appear that in children the attack is in any way different from that in adults. Evidently the chance of infection among very young children is small, though in Patterson, N. Y., two recent cases involved a mother and her 21 months old baby. Cases of prenatal infection have been recorded, however. But this could hardly be severe in any instance, because of the limited number of embryos that could gain access to the fetus.

Prevention of Trichinosis.—Man acquires trichinosis by the consumption of pork products containing living larvæ. Microscopic examination of meat at slaughter houses does not adequately protect the public. Methods of salting, smoking and otherwise curing these products do not certainly kill the trichinæ, but a temperature of 131°F. (55°C.) insures the death of the parasites. It should be remembered that only prolonged cooking will raise to this level the center of a piece of meat. A uniformly clear gray color and the absence of red juice under pressure of the knife shows that a temperature of at least 60°C. has been reached. The consumption of well cooked pork is free from danger.

Ancient methods of slaughtering in which refuse was thrown uncooked to pigs and fell in part also to rats furnished unsurpassed conditions for the multiplication of trichinæ. In modern packing houses the utilization of all waste in processes that insure the death of any parasites has been an influential factor in the reduction of the numbers of this dangerous parasite. Freezing to 5°F. (−15°C.) for 20 days results also in the destruction of the parasites and aids further in the general hygienic advance. The relinquishment of the habit of eating pork products uncooked is the most reasonable and most effective individual prophylaxis.

Treatment.—The stage of diarrhea at the onset of the disease is usually missed. If recognized the chance of recovery is 80 per cent. greater. Early abortion of the disease may in the less severe case be effected by symptomatic treatment, such as rest in bed, gastric lavage, and the administration of thymol: orally, for a 10 year old child, in dose of ¾ gr. four or five times in the first 24 hours, followed always by a saline purge to reduce toxicity. There is no specific remedy for trichinosis. In a severe case, the patient should be given the benefits of general hygiene and relief from pain and sleeplessness.

Convalescent serum gave good results in 14 cases, according to Salzer, but Schwartz and Alexander obtained negative results. Nieto reported seven cases of trichinosis treated by intravenous injection of neosalvarsan [dose in a child, 0.015 gm. for every kilogram (2.2 lb.) of body-weight]. Prompt recovery took place usually after two or three injections. Glycerin, for a 10 year old child, 30 minims every hour with laxatives, gives good results because of its hygroscopic quality.

SUBORDER STRONGYLOIDEA Weinland 1858

The Strongyloidea are distinguished by the presence in the male of a broad bursa, traversed by a system of rays. Of these six are paired and one median and unpaired, but all radiate outward from a common center. The mouth is surrounded by six papillæ. A spherical buccal capsule is usually developed in both sexes, but may be wanting. This large and complex group, which was formerly regarded as a family, is now treated as a suborder and divided into a number of families which contain some of the most serious of human parasites. Three families are of medical importance: Strongylidæ, Trichostrongylidæ, and Metastrongylidæ.

FAMILY STRONGYLIDÆ Baird 1853

Well-developed buccal capsule. Oviparous, with thin-shelled, transparent eggs, parasites of the alimentary canal.

The family includes some dangerous blood sucking parasites among which are the human hookworms. Two genera are represented, commonly called the Old World and the New World Hookworm. The anterior end is curved dorsal and the mouth opens obliquely from a large buccal capsule armed with teeth or cutting plates.

GENUS ANCYLOSTOMA Dubini 1843

Synonym.—Dochmius Dujardin 1845.

On the anterior ventral margin of buccal capsule two pairs of large uncinate teeth, turned inwards. Within capsule one median and two short bilateral ventral cutting plates.

The name has been spelled in a score of different ways. The form used here has been finally adopted by the International Commission on Zoological Nomenclature and should be universally employed.

Ancylostoma duodenale Dubini 1843

Synonyms.—*Agchylostoma duodenale* Dubini 1843; *Anchylostoma duodenale* Dubini 1850; *Strongylus quadridentatus* von Siebold 1851; *Dochmius ankylostomum* Molin 1860; *Sclerostoma duodenale* Cobbold 1864; *Str. duodenalis* Schneider 1866; *Dochmius duodenalis* Leuckart 1876; *Uncinaria duodenalis* Railliet 1885; *Ancylostoma* and *Ancylostomum duod.* auct.

The body (Fig. 383) is cylindrical, only slightly tapered at the ends, pale flesh-colored in life, white or gray in alcoholic specimens. The female measures 10 to 13 by 0.5 to 0.8 mm. The vulva is at or near the posterior third of the body; the eggs are colorless, thin-shelled, 56 to 61 by 34 to 38μ, usually in the four-cell stage in fresh stools; development is direct. The male measures 8 to 10 by 0.4 to 0.5 mm., having a caudal bursa with a dorsomedial lobe, dividing at two-thirds the distance from the base, each branch tridigitate, and with prominent lateral lobes united by a ventral lobe; the spicules are long and slender.

In the adult are voluminous glands: cephalic, cervical, and in the male anal also. Next to the buccal capsule, these are the most conspicuous and characteristic features of the worm.

Distribution.—This species lives in the upper portion of the small intestine of man and has been bred also experimentally in puppies, kittens and monkeys; older animals of these species are resistant to it.

The parasite is primarily European in distribution but occurs, though less frequently, in Asia, Africa and America, very likely having been distributed there by Europeans. Although ordinarily few in number, up to 1000 have been found at one necropsy. The worm is long-lived and clinical studies set its limit of life at from five to six years.

Life History.—The eggs are deposited in the alimentary canal of the host and when evacuated with the feces, are usually in the four-celled stage; in the outer world they develop rapidly in feces or in moist earth so that the rhabditiform embryo is hatched in 24 hours at 27°C. However, a lower temperature retards the process and frost or 1°C. kills the eggs in from 24 to 48 hours, setting an evident climatic limit to the spread of the species. Complete drying of the feces or of the infected soil and direct sunlight are fatal, also. More than 99 per cent. perish in nine weeks at 27°C., and at 35°C. all were dead in three weeks.

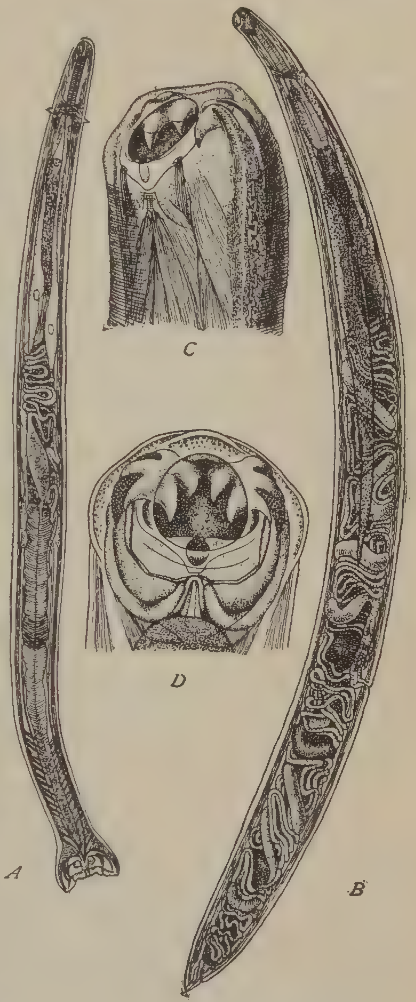

FIG. 383.—Old World Hookworm, *Ancylostoma duodenale; a*, adult male, ×15; *b*, adult female ×15; *c*, head of male from right side, ×140; *d*, same in ventral view, ×100. (After Looss.)

The larva just hatched from the egg is from 0.2 to 0.25 mm. long by 0.015 to 0.017 mm. broad. The rhabditis form of the esophagus, *i.e.* with three regions, is characteristic as well as the long cylindrical buccal cavity which is lined by a thick highly refractile membrane. The rudiment of the reproductive system appears as a large clear cell at the end of the center third of the body. The anus lies some distance in front of the point of the tail. After from three to five days of growth in the fecal matter, the larva molts (Fig. 380) without any conspicuous change in form or structure, but after some days of further growth, when it has reached the length of from 0.7 to 0.8 mm., the form of the buccal cavity and of the esophagus characteristic of the early stage is lost, but it becomes more slender (strongyloid type) and a second molt occurs. At this time the old cuticula is not cast off but remains as a sheath around the body. In this condition the larva is often erroneously spoken of as encysted. It remains in the mud or water without appreciable change and without taking food for some two to three or at most four months in the soil at least. It is the only stage in which the infection of man can be brought about.

Looss first demonstrated that these larvæ enter the skin, usually of the hands or feet, which in many ways naturally become smeared with mud containing the worms; yet when taken into the mouth with contaminated water or uncooked food they may bore into the mucosa and start the same migration within the body as if introduced through the external skin. The infection of field laborers, workers in mines and brickyards, and of children walking barefooted in damp soil is readily explained by this phase in the life history, as is also the mild dermal irritation, or "ground itch," long since observed in regions where hookworm disease is frequent. The typical lesion in this malady consists in a primary erythema succeeded by a vesicular eruption, which frequently becomes pustular and in severe cases results in ulceration or even gangrene.

Once having entered the human tissues, the larvæ penetrate blood- or lymph-vessels and are carried through the heart into the lungs, when they desert the blood system, enter the pulmonary alveoli, migrate outwards along the air passages into the pharynx and down the esophagus, reaching ultimately the duodenum. Here growth and transformation especially of the buccal capsule brings about the adult form. In from three to seven days the third molt produces the fourth stage, and in 13 days the fourth and last molt leads to the fifth and final stage. Three to four weeks bring sexual maturity and the completion of the life cycle.

As the other species of human hookworm is not always distinguished from Ancylostoma, it will be described before hookworm disease is discussed.

GENUS NECATOR Stiles 1903

Buccal capsule relatively small; in place of marginal teeth, dorsal and ventral pair of lancets deep in capsule. Orifice of dorsal gland on conical projection from dorsal wall of capsule, projecting freely into buccal cavity.

Necator americanus (Stiles 1902)

Synonyms.—*Uncinaria americana* Stiles 1902; *Ancylostoma americanum* Verdun 1907; *Ank. duodenale* (older references in part); *N. argentinus* Parodi 1920.

The oral capsule (Fig. 384, *a*) is relatively small and spherical. There are no ventral recurved uncinate teeth in the buccal cavity; the dorsal semilunar plates are prominent, the ventral pair inconspicuous (Fig. 384, *b*). The female measures 9 to 11 by 0.31 to 0.35 mm. The vulva is near the center of the body *but in front of it.* The ova measure 64 to 72 by 36 to 40 μ. The male measures 7 to 9 by 0.29 to 0.31 mm. The spicules are 0.92 mm. long, partially united; there is a caudal bursa with relatively strong ribs, and the dorsal ray of the bursa is divided to the base, each branch bipartite to the tip.

Distribution.—This species lives in the small intestine of man and of the African apes. It was originally described by Stiles from material sent him from Porto Rico by Ashford, and is widely distributed on the

American continent. Its presence among the pigmies in the forests of central Africa as well as among various African tribes has led to the belief that it was originally a parasite of that continent and was introduced into the Western world by the slave trade, being most abundant in regions directly affected by that (Gulf States, Antilles, Brazil). In the South it is not a recently imported parasite but has been endemic for many years, though not previously recognized. The older records confuse completely the two species. It is reported from Australia, Samoa, and other Polynesian islands. It has been found also in Asia and in the East Indies. Its introduction into some places in Europe (Italy, Switzerland) has been directly traced to emigrants returning from Brazil.

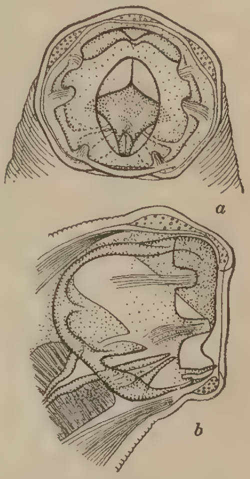

Fig. 384.—New World Hookworm, *Necator americanus*; *a*, head of male in dorsal view, ×160; *b*, head of female from the right, ×160. (After Looss.)

Cobb has shown that the larva of *N. americanus* has a protrusible boring spine and three esophageal glands with separate ducts.

The life history, as worked out by Claude Smith and others, is similar to that of *Ancylostoma duodenale*. Experimental animals are not readily infected; the pig and dog not at all. The bionomics of the free stage have been carefully worked out by Cort* and his associates.

Differentiation of Types of Hookworm.—The difficulty of differentiating the two hookworms calls for a tabulation of the structural differences for use in microdiagnosis. Some of these are discernible only if both species are at hand for immediate comparison.

Table 13.—Structural Differences of Hookworms

Ancylostoma	Necator
Prominent hooks in buccal capsule	Semilunar plates prominent; hooks wanting
Vulva well behind center of length	Vulva near, but in front of center of length
Fine spine at posterior tip of female	No spine at posterior tip of female
Posterior tip of male bent in continuation of general body curvature	Posterior tip of male bent in opposite direction to general body curvature
After death, head bent in continuation of general body curvature	Head hooked sharply in opposite direction to general body curvature
Eggs shorter but equal in thickness to those of Necator	Eggs distinctly longer but of equal breadth to those of Ancylostoma
Body thicker and a little longer than Necator	Body more slender and shorter than in Ancylostoma

Hookworm Disease.—Climatic Distribution.—As the worms require a moderately high temperature to complete the life cycle, and a considerable amount of moisture, the disease is rampant in those parts

* Cort, W. W., Investigations on the control of hookworm disease, xxxiv. General summary of results. Am. J. Hygiene, v (Jan., 1925), pp. 49–89.

of the tropical and subtropical zone where humidity prevails. In temperate regions the parasites occur irregularly, and only where conditions are favorable, as in mines. In infested regions the prevalence of the disease is often very high and shown by the table of frequency taken from Brumpt and others (Table 14).

TABLE 14.—PREVALENCE OF HOOKWORM DISEASE

Country	Percentage infected	Authority
North China	11.0	Bowman and Saylor
Loochoo (Japan)	84.3	Hoki
Korea	34–39	Kojima and Ko; Kwum and Kobayashi
Indo-China (Tonkin)	39–62	Mathis and Léger
North Siam	94.0	W. F. Kerr
Philippines	31–52	F. Garcia; Garrison
Borneo	59.0	Christie and Ledingham
British East Indies	43–46	R. W. Chester
East Indies	52–83	Garrison; Calvert
Africa-Egypt	10–69	Wenyon and O'Connor
Egypt (cities) boys	22.7	Int. Health Board (1915)
Egypt (villages) boys	51.1	Int. Health Board (1915)
Congo	high	Many writers
Guinea	75.3	H. Clapier
Victoria Nyanza	49.5	N. P. Jewell
South America:		
Amazonas (Brazil)	95.2	Da Matta
Central America:		
Costa Rica (children)	91.4	H. R. Carter
Honduras	79.25	N. Barlow
Porto Rico	75.0	Hookworm Commission
Porto Rico (less than 10 years)	11.0	Ashford and Guitierez
Panama (city) children	24.4	Int. Health Board (1914)
Panama (interior) children	69.1	Int. Health Board (1914)
United States:		
Georgia	18.6	Willets
Texas	57.6	J. H. Frey
Texas	28.86	Judkins
Texas (children)	39.0	Judkins

Hookworm in America.—The percentage of infection in various regions of America is high, varying from 18 per cent. of persons examined in some southern states to 90 per cent. of the population of Porto Rico. A survey of campaigns in 11 southern states covering 81 counties and lasting five years yielded the highest infection rate among rural school children between 6 and 18 years, of whom about 90,000 were originally examined and nearly 50,000 found infected (55.1 per cent.). At the re-examination 12,236 out of 44,090 were reported infected, and the reduction in severity was undoubtedly very much greater.

The development and mode of infection of *Necator americanus* agree so far as known with that of the old world hookworm, *Ancylostoma duodenale*.

Diagnosis of Hookworm.—Positive diagnosis of hookworm disease is made by identification of parasites or eggs in the feces. Owing to similarity of eggs in other species to those of hookworm confusion is readily possible (cf. Trichostrongylus). The direct examination of feces, followed by the centrifuge treatment described in detail by Howard, has not proved sufficiently accurate. Darling worked out a method depending on the fact that ova float in a mixture of one part glycerine and two parts saturated solution of sodium chloride. A still better method is the Willis as modified by Mallory. In the special apparatus a small quantity of feces is mixed under set conditions and the container covered by a slide. The parasite eggs immediately rise to the surface and adhere to the glass whereupon the slide is removed and the ova are studied under a microscope. Tests are rapidly made and are more accurate for hookworm infection but less so for Ascaris, and most inaccurate for larvæ, either of hookworm or Strongyloides.

Incidence in Children.—While earlier writers were much inclined to emphasize the special significance of hook-worm disease for children, Smillie* states that it is essentially a disease of youth. His studies were conducted in Brazil and are the most critical inquiry of this phase yet made. Few children less than six years of age were studied and none less than four years. The greater part of them were children of field laborers, and had never been to school or worn shoes or been five miles from the place of their birth. The results are shown in Table 15. According to Smillie's recent studies in the South clinical hookworm disease is almost limited to children of school age.

Table 15.—Hookworm among Children in Brazil

Age, years	Boys		Girls	
	Number cases	Average number hookworms	Number cases	Average number hookworms
4–5	3	1	3	0
6–7	8	20	11	12
8–9	18	52	14	31
10–11	19	113	17	54
12–13	28	185	21	101
14–15	59	184	20	87
16–17	53	106	23	158
18–19	22	167	12	197
20–24	36	260	26	108

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* Smillie, W. G., Studies on hookworm infection in Brazil. Monogs. Rockefeller Institute No. 17, New York (1922).

Prenatal Infection.—De Faria has discovered hookworm eggs in the stools of children only three or four months old and is inclined to explain such cases as due to placental infection. Howard found ova in the feces of a child only 14 days old and calls attention to the fact that, if the infant had been infected at birth, it could not have shown ova in the stool before the end of the fourth week; hence the infection must have been prenatal. The mother had ova in her stool and gave a history of ground itch during pregnancy.

It appears that younger children are only slightly infected, but the infection increases rapidly after eight years, in boys and girls alike when the children begin work in the field. The degree of infection also increases markedly at the same age-period. Furthermore, when the children were divided into two groups, those who worked in the fields and those who did not, but comparable in all other respects, the increase in hookworm infection was slow in the second group and very rapid in the first group, so that at 14 years of age the degree of infection was six times as great among children working in the fields as among the nonworkers. The average hemoglobin of the two groups is at that age almost 15 points apart.

Chronicity of Infection.—Hookworm infection is gradually acquired. As the Table 15 shows, children four years old have almost no infection, at five they have on the average three worms, at seven from 15 to 20 worms, at nine years 30 to 50 and at 10 the average country boy (in Brazil) shelters 60 hookworms. It has been shown that the hookworm lives five or six years, hence that infection represents an accumulation of about 10 worms a year. After the boy begins to work in the field the increase averages 50 hookworms a year. Mass infection is acquired over a longer period of years, and the infections of childhood begin to demonstrate their significance only after the host has reached youth or young adulthood. Once acquired, the infection is only slowly lost; thus after four years under perfect sanitary conditions, one girl still harbored 369 hookworms. In Porto Rico, Cort and his associates found that children are only slightly infected up to the age of eight, but the curve of infection shows very rapid increase from 8 to 11, reaching then the figures for adult women. The boys continue to show an increase up to 19 or 20 when they have an infestation more than twice as heavy as women.

The average normal hemoglobin for children from 5 to 14 years old is 68 per cent. An average of 25 hookworms per case does not lower the children's hemoglobin, but the reduction with greater numbers of hookworms becomes ultimately twice that produced under the same conditions in adults.

Pathology.—The effects on the human host induced by the two species are substantially alike. The worm attaches itself firmly to the intestinal wall and by virtue of the powerful armature of the buccal capsule, either recurved teeth or cutting plates, removes the epithelial layer over a considerable area. From the denuded surface comes an extravasation of blood which is continuous even after the parasite has moved to another spot. It is believed that the secretions of the large glands inhibit the coagulation of the blood and thus induce the continuous hemorrhages from the intestinal surface. The anemia characteristic of the disease is explicable on the basis of the loss of blood, but some hold to the view that the parasite produces a toxic substance which affects the host unfavorably. Certain it is that elimination of the parasites is followed promptly by favorable changes in the condition of the host. The disease develops slowly.

Symptoms.—Hookworm disease or ancylostomiasis is also known as tunnel disease, brickmaker's or miner's anemia and Egyptian chlorosis. The chief symptoms are progressive anemia, with erythrocytes often less than one million, the circulatory disturbances accompanying the pernicious type; colicky pains in the abdomen; great weakness; alternating constipation and diarrhea with brownish or bloody stools; nausea; edema; mental depression, and marked apathy. In children a noticeable symptom is "pot-belly."

Effect on the Child.—Extreme cases are easily recognized and have been much discussed. Mild cases of hookworm disease in children are often entirely overlooked as the characteristic symptoms are lacking, though the effects of the parasite are no less real. Typical mild cases are recorded by Frazer* who, after a course of treatment, reported marked improvement in a few weeks. Teachers testified that many such children after treatment "were transformed from dullards into normal, mischievous children." However, Stiles concluded that light infections had no effect on the mental powers of the children harboring hookworms. On the other hand, the studies of Waite and Nelson in Australia revealed that "slightly infected children averaged 5.4 months by the Binet test, and two months by the Porteus test, lesser mentality than their hookworm-free associates, while heavily infected children showed by comparison with hookworm-free, an average reduction 19.5 months by Binet and 13.3 months by Porteus. The longer infection lasts, the greater is the mental retardation. Mental sluggishness is revealed by all three tests." While these authors consider that the hookworm is stamping serious mental, physical and sexual degeneracy on 25 per cent. of the total school population of Australia, the International Health Board is authority for the statement that the examination of several thousand school children in selected state schools of Australia revealed an exceedingly low percentage of hookworm disease. Some reports of examinations of individual regions depart widely from this general statement. More extended studies are essential before final conclusions can be reached.

During 1918–1921, a thorough examination for hookworm was made of 95 per cent. of the population in the coastal belt of North Queensland. Lambert called attention to the very high proportion of infections among the children, particularly of ages between 8 and 12. He attributes this partly to the fact that children go barefooted, and partly to the newness of the infection. Yet the adults of the present generation were surely not so severely infected during their early years as are children in the same district today.

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* Frazer, Thompson, Mild cases of hookworm disease in children. J.A.M.A., lvii (Sept. 2, 1911), p. 791.

The International Health Board.—Considerable sums of money have been devoted to the study of hookworm disease and to the movement for its eradication. In this campaign significant results have been secured, and marked progress has been made toward a knowledge of the disease and a reduction in its effects. As regards children, it appears that hookworm disease is much lighter in cities than in small towns and in the country. This holds true even of tropical environment. In Panama City about 25 per cent. of the children between 6 and 17 years of age examined for hookworm were infected; whereas in the interior, nearly 70 per cent. of the children examined, of the same ages, were infected. In Costa Rica the percentage of infection among children of the same ages surpassed 90 per cent. Infection was recorded in 39 per cent. of microscopic examinations among 550,000 rural children in the United States.

The studies of the International Health Board on the effects of hookworm disease on the mental and physical development of children indicate that hookworm disease interferes with physical development and that treatment will alleviate this condition to a considerable extent. Young children can apparently regain most, if not all, of what has been lost through the infection, the permanency of the ill effects being directly related to the severity of the infection and the length of time it persists. More serious retardation follows sickness between the ages of 5 and 10 than later.

It appears also that hookworm disease affects definitely mental development, and the mental condition is not benefitted by treatment to the same extent as is the physical condition. Prolonged infection may produce effects from which the individual may never entirely recover.

Darling, in writing of the Orient, emphasizes the important fact that the worm index is the only reliable guide, both to the number of persons infected and to the heaviness of infection. Usually men have the highest worm index, then boys, women and girls in order; but on rubber estates where Tamil women work on the trees while men and children work indoors the order is reversed.

Hookworm Infantilism.—Lehmann has enumerated the characteristics of the type of infantilism seen in hookworm disease: (1) A general retardation of growth, symmetrical and harmonious; (2) a simple retardation of skeletal changes; (3) a failure of development of the genitalia as well as an absence of secondary sexual characteristics; (4) a mental slowness and dullness (not always present), and (5) a general appearance which conforms neither to the Brissaud nor to the Lorain type.

Treatment of Hookworm.—**Thymol.**—World-wide hookworm campaigns have led to the intensive study of anthelmintics. Thymol, the classic remedy, is highly toxic and occasionally causes death;

one-half to two-thirds of it is absorbed by the alimentary canal. Its solubility in oil complicates the problem, and at times its lack of efficiency after repeated doses is a serious handicap. The treatment, as outlined by Osborne and Fishbein, is:

> Give little or no supper, and at bedtime a dose of magnesium sulphate. In the morning, as soon as the bowels have moved freely, one-half dose of thymol, placed dry in capsules, uncapped before swallowing, is given, and in two hours the remainder. At 15 years the dose is 12 gr., and at 10 years 8 gr. In the child less than five years old, Smillie asserts that the difficulty of treatment and the danger to the child exceed any advantage following the removal of the worms. Maltose may be added in equal parts to the thymol. The dose should be given with plenty of water. Nothing except water should be allowed until the thymol has passed out of the body. Alcohol and oils should not be given either before, during or soon after treatment. For one hour after taking thymol the child should lie on the right side to hasten the passage of the drug and water through the pylorus into the intestines. Repetition of treatment may be necessary in one or two weeks, or even three or four treatments. unless the microscope shows no eggs in the feces.

Poisoning.—To forestall poisoning, a brisk cathartic (Epsom or Rochelle salt) should be given in all cases one hour after the last dose of thymol is taken. The symptoms of poisoning are weakness and collapse, with albumin and blood in the urine. To treat thymol poisoning, give sodium sulphate or potassium and sodium tartrate to promote elimination, sodium bicarbonate to counteract acidity, and wash out the stomach and colon. Hypodermic injections of atropin sulphate (1/200 gr. in a 10 year old child), strychnin nitrate (1/100 gr.) or liquor hypophysis (eight minims) will have a stimulating effect. Surround the patient with dry heat. The later kidney congestion should be treated as acute nephritis.

Carbon tetrachloride has recently come into general use. It appears to be the most efficient vermifuge for *Necator americanus*, removing from any large series of cases 95 per cent. of the worms by the first dose giving complete cures in a majority of cases and clinical cures in practically all. As a result of experimental tests with carbon tetrachloride, Nichols and Hampton* report that it may be administered safely in doses of from 10 to 20 minims to children of three and four years of age, including those seriously ill. Even one year old infants may be given 10 minims with safety, and this dose should be increased by two minims for each year of apparent age. Thus a child of 10 would receive 28 minims, and a youth of 16 would receive 40 minims (2.5 cc.). Carbon tetrachloride is a mild laxative but cannot be depended on to move the bowels when used in moderate doses. It is good practice to give a saline purge one or two hours after administration of the drug in all cases.

Poisoning.—The majority of fatal cases reported for carbon tetrachloride in the past have been among children with heavy ascarid infection and among alcoholics. Death is due to central necrosis of the liver, as in chloroform poisoning, with necrosis of the suprarenals, with evidence pointing to toxic effects on the nervous system due to toxins from dead or injured ascarids.

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* Nichols, L., and Hampton, G. G., Treatment of hookworm with carbon tetrachlorid. Brit. M. J., ii (July 1, 1922), pp. 8–11.

Oil of chenopodium or wormseed oil is apparently the most effective drug against *Ancylostoma duodenale* being perhaps slightly more effective than carbon tetrachloride. Recently N. C. Davis reported on the treatment of hookworm by a mixture of eight parts of carbon tetrachloride and one part of ascaridol, the active principle of oil of chenopodium, administered in a dose of 0.2 c.c. per year of age to children less than 10 years old. No serious intoxications were recorded in a series of more than 500 treatments in children. This mixture is also efficient in cases of infection with Ascaris. Chenopodium 1 part and carbon tetrachloride three to four parts is highly effective against hookworm, both Necator and Ancylostoma, and is the indicated combination for hookworm cases complicated with ascariasis, especially if the latter is severe. The combination should in all cases be followed by salts an hour later. Since oil of chenopodium is highly constipating,* it must be followed in one hour by a saline purge. This not only removes the worms but affords a high degree of protection against the poisonous and constipating effects of chenopodium.

Poisoning.—Possible undesired symptoms from wormseed oil, such as drowsiness and depression, may be overcome by a rapid purge with a saline cathartic and hypodermic stimulation by caffein sodiobenzoate, 1½ gr. in a child aged 10 years.

OTHER SPECIES OF HOOKWORM IN MAN

Ancylostoma braziliense a parasite of the dog in Brazil, has been found occasionally in man. An eastern canine parasite, described as *Anc. ceylanicum* and reported as an occasional human parasite in India and Siam, is in reality the same species. It occurs in company with *A. duodenale* and is easily confused with that species. While not common, it is found in children, both native and European, as well as in adults.

Necator suillus, discovered in the pig in Trinidad closely resemble *N. americanus* and has often been confused with it. The relation of this species to man is not yet determined.

GENUS ŒSOPHAGOSTOMA Molin 1861

Greatly inflated buccal capsule reduced to chitinous ring and cut off from body by nuchal furrow. Vulva near the anus. Male has two equal, slender spicules and two prebursal papillæ.

Oesophagostoma brumpti (Railliet and Henry 1905)

The immature female measures 8.5 to 10.5 by 0.3 to 0.33 mm. The oral crown of twelve pointed lamellæ is directed anteriad and centrad. There are six oral papillæ. The ova measure 30 by 27μ.

This species was discovered at necropsies of negroes in East Africa and Guinea. The wall of the cecum and colon contained nodules the size of a pea or bean, in which the immature worm was found in the midst of a hemorrhagic mass. With sexual maturity the worms emerge into the intestinal lumen, doing marked damage to the wall, especially in the event of a heavy infection. The species lives also in several monkeys of the region.

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* Sawyer, W. A., and Sweet, W. C., Comparison of certain methods of treatment and diagnosis of hookworm infection. Arch. Int. Med., xxxiii (Jan., 1924), p. 35.

Oesophagostoma stephanostomum var. thomasi (Railliet and Henry 1909)

The immature females are from 16 to 20 mm. long and 0.9 mm. broad at center, tapering towards both ends. There is an oral crown of 38 semicircular lamellæ with a circle of 76, short, chitinized teeth. The male measures 17 to 22 by 0.75 mm., with spicules from 1.38 to 1.48 mm. long.

This worm was discovered in Brazil at the necropsy of a prisoner from Manaos. Many tumors on the walls of the large and small intestines held each a single worm. Other closely similar forms of the same species have been obtained from the gorilla and chimpanzee. The South American host was sought in vain. The worm is only an accidental parasite of man.

Another record of an unidentified species of this worm, from a native of western Africa, suggests that these forms, which are normal parasites of monkeys and apes in many regions, frequently become accidental parasites of man. The tumor-forming habit makes them dangerous guests in the human organism.

GENUS TERNIDENS Railliet and Henry 1909

Distinguished from Œsophagostoma primarily by lack of inflated buccal capsule. Three teeth project into capsule at base. Margins of bursa dentate. Vulva near posterior end.

Ternidens deminutus (Railliet and Henry 1905)

Synonyms.—*Triodontophorus dem.* Railliet and Henry 1905; *Globocephalus macaci* Smith, Fox and White 1908.

The body tapers regularly to both ends. The mouth is elliptical; the chief axis is dorsoventral. The oral ring has from 22 to 24 lamellæ. There are two large lateral and four small, submedian, oral papillæ. The male is 9.5 mm. long and 0.56 mm. broad. The bursa is broader than long. The female is from 12 to 16 mm. long and 0.65 mm. broad. The vulva is 0.68 mm., the anus 0.27 mm. from the posterior tip. The ova measure 64 to 70 by 39 to 40μ.

The first specimens from man were obtained at Mayotte in 1865. Brumpt found it later in Asiatic monkeys (Macacus). It was also obtained in 1908 at necropsies of natives of Nyassa. The species is of especial importance in America as A. J. Smith recorded it from Macacus in the Philadelphia Zoological Garden.

Other Strongyles Occasional in Man.—The gape-worm (Syngamus) was reported by Leiper as a human parasite in St. Lucia. The species was called *S. kingi* but later said to be probably *S. laryngeus* which Ransom states is common in the West Indies.

GENUS TRICHOSTRONGYLUS Looss 1905

Slender worms without buccal cavity; mouth provided with three small lips, sometimes also with papillæ. Male bursa bilobed; median lobe insignificant; spicules short, twisted in form of spatula, with accessory piece. Vulva in posterior half of body; uteri divergent; ovijectors well developed. Eggs, thin-shelled, when laid, contain from 8 to 32 cells.

Trichostrongylus colubriformis (Giles 1892)

Synonyms.—*Strongylus instabilis* Railliet 1893; *S. subtilis* Looss 1895; *Tr. instabilis* Looss 1905.

The body is very slender and delicate; the oral papillæ are inconspicuous; the buccal cavity is funnel-shaped; the esophagus is about one-sixth of the body length. The male has minute alæ at the anterior end; is from 4 to 5 mm. long; with spicules 0.15 mm. long and an accessory piece 0.05 mm. long. The female is from 5 to 7 mm. long, with sharply pointed tail; the vulva is about one-fifth body length from the posterior tip. The eggs are oval, measuring 63 to 80 by 41 to 36μ, containing from 20 to 30 cleavage cells when laid.

This worm was originally described as a human parasite from necropsies in Egypt. It appears in the East to be frequent in sheep as well as in man. The worm inhabits the duodenum near the pylorus, and the infection is usually so light that its pathogenic character may well be doubted even though in sheep it gives rise to pernicious anemia. The eggs are so much like those of the hookworm in size and appearance that confusion is very probable. The species has been identified in Japan in the human host, and in India in sheep. It is very common in sheep and cattle in the U. S. A. according to Ransom.

Trichostrongylus orientalis Jimbo 1914

Synonym.—*Strongylus subtilis* Looss 1895 pro parte.

This may be distinguished from related species by the arrangement of the bursal rays and by the size of spicules in the male. It is apparently frequent as a human parasite in Japan, Korea, and Formosa. The ova are often confused with those of the hookworm and the worms themselves with *Tr. colubriformis.* The worms are ordinarily of no pathologic import, but when present in such large numbers as reported by Ogata, *viz.*, 200 in the one case, they may be assumed to have some significance.

Trichostrongylus probolurus (Looss 1905)

Synonym.—*Strongylus probolurus* Railliet 1896.

This is much like the last two species and was found in the duodenum of Egyptian peasants by Looss. It is not distinguishable in effects or importance from the previous species. Since it has been reported in other hosts in this country, one may expect it to occur at some time in the human host.

Trichostrongylus vitrinus Looss 1905 is the rarest of the group. Resembling these previously noted in structure, and probably similar in its effects as well. It is also found in the U. S. A.

Mecistocirrus fordi (Daniels 1908) is a normal parasite of the pig and cattle in Asia which may be found accidentally in man. It inhabits the alimentary canal. The reports of its presence in the human host, which come from the far East, are lacking in details.

Hemonchus contortus (Rudolphi 1803) is an intestinal parasite of sheep, goats, and cattle. When abundant it produces a pernicious anemia due to its blood sucking habit. Magalhães has encountered it in man in Brazil. The patient suffered from severe anemia, supposedly due to hookworm, and was promptly relieved by the elimination of the parasite. The case offers an interesting demonstration of the similarity of clinical symptoms which may be induced by different helminthes, and the possibility of confusion, with other species. This parasite has also been reported from West Australia where Sweet found three cases in natives.

SUBFAMILY METASTRONGYLINÆ Leiper 1908

The Metastrongylinæ are polymyariæ. The buccal capsule is small or wanting and in development a rhabditiform embryonic stage is lacking. These forms occur in the respiratory or circulatory system.

The genus Metastrongylus Molin 1861 includes parasites that inhabit the bronchi of the pig and only by some rare accident parasitize the human species. One of the forms, *M. apri* (Gmelin 1789), is exceedingly common in the pig in Europe and may produce a fatal bronchitis in young animals. It has been reported twice in the human host. In 1845 Diesing stated that Jortsits had found it in the pulmonary tissue of a boy of six years in Transylvania. Other later cases probably involve this species.

SUBORDER ASCAROIDEA Railliet and Henry 1915

These nematodes have the mouth guarded by three lips, usually supplied with papillæ but without a buccal capsule. The female has two ovaries and is regularly oviparous. Development is direct. This is a large group with species that are important parasites in all types of vertebrates. Only two families of the suborder are important in human parasitology, the Ascaridæ and Oxyuridæ.

FAMILY ASCARIDÆ Cobbold 1862

Polymyaria; relatively thick, heavy body, with three prominent lips one dorsal two ventro-lateral. Three interlabia present. Esophagus long, muscular, inflated at distal end, often provided with esophageal bulb. Male usually has two spicules, female an abruptly conical posterior end and double ovary. Oviparous, development direct though accompanied by migration in body of host. Intestinal parasites.

GENUS ASCARIS Linnaeus 1758

With prominent and often complex lips without fringes or tentacles on margin. Male with two equal spicules and many pre-anal and postanal papillæ. Vulva in front of center of body. Many species, three from human host.

Ascaris lumbricoides Linnaeus 1758

The body is pink or gray-yellow in the living worm and spindle-shaped. The lips (Fig. 385, *a*, *b*) are nearly alike, roughly semicircular, with fine marginal teeth, with two papillæ on the dorsal lip and only one each on the ventral lips. The male is from 15 to 17 or, rarely, to 25 cm. long and 3 mm. thick. The posterior end is curved ventrad; the spicules are 2 mm. long; there are from 55 to 60 pre-anal and seven pairs of postanal papillæ. The female is from 20 to 25, or even 40 cm. long, and from 5 to 5.5 mm. thick, with a straight, conical, posterior tip. The vulva is located in a depression at the end of the first third of length. The ova are elliptical, with a transparent mamillated layer covering the shell; they measure 50 to 75 by 40 to 58μ and are laid before cleavage begins. The unfertilized eggs are irregular, with a scanty albumen layer, coarser protoplasm and thinner shell, and measure 81 by 45μ (Fig. 386).

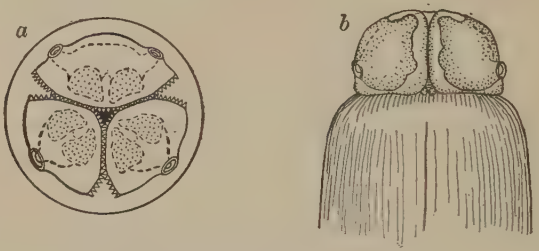

FIG. 385.—Head of *Ascaris lumbricoides; a*, from in front; *b*, from the side. Magnified. (After Leuckart.)

Distribution.—This parasite, known as the common roundworm or stomach worm of children, is cosmopolitan in its distribution. Though more abundant in warm regions, it has been reported from Finland and Greenland and lives in all latitudes and climates. It probably has a wider geographic distribution and infests more people than any other known parasite (Tables 1–4). Owing no doubt to its abundance in the pig this species is a country parasite and is rare in city dwellers. It has been known as a human parasite since ancient times, being recorded in medical writings of both Greek and Romans; but the form designated by the same name in Greek (ἀσκαρις) is that now called Oxyuris.

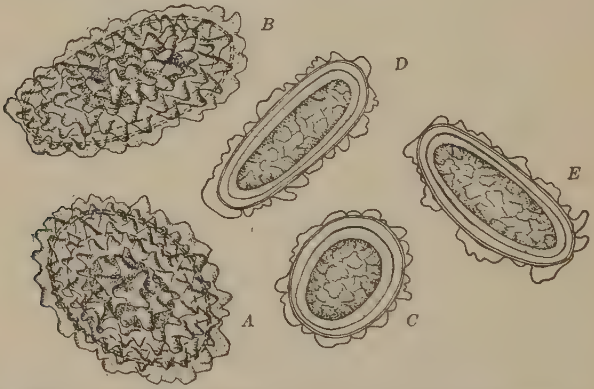

FIG. 386.—Eggs of *Ascaris lumbrĭcoides; a*, normal surface aspect; *b*, elongated egg; *c, d, e*, optical sections of *a* and *b*. *a* and *b*, ×420, *c. d. e*, ×280. (After W. D. Foster.)

The Egg.—The structure of the egg is striking and among all human parasites peculiar to this species. The exterior is mamillated, and this appearance is due to a transparent albuminoid layer deposited on the exterior of the true egg shell. One finds in some cases ova that are noticeably longer and narrower, with a scanty irregular albuminoid covering and with more coarsely granulated protoplasm; these are believed to represent unfertilized eggs. However, normal ova vary considerably in these particulars and it is claimed that all varieties may be met in a stool from a single patient.

When discharged from the body of the host, the eggs are still undivided and must be incubated for a period depending on the external temperature before they become capable of infecting a proper host. They may be cultured in tap water and even more successfully in 2 per cent. formalin, which inhibits bacterial growth without affecting the activity of the egg itself on account of the impermeability of the shell.

Eggs of *Ascaris lumbricoides* are highly resistant to unfavorable conditions. They withstand low temperatures and considerable desiccation for long periods. They survive for more than a month in urine and continue to develop even in a strong solution of salt and in powerful preservatives.

Life History.—Cleavage begins after the eggs are discharged from the host and the development of the embryo under most favorable circumstances of moisture and warmth requires from 30 to 40 days, though Wharton reports that at room temperature Ascaris embryos develop from freshly laid eggs in 10 days. The full-grown embryo does not desert the egg shell but lies within it coiled in a spiral, even after the first molt, until it is introduced by chance into the alimentary canal of the human host, when it is set free by digestion.

The earlier view that the development was direct and the intervention of a secondary host unnecessary has been substantiated fully by recent experiments, but these have demonstrated certain unexpected occurrences which explain the confusion in earlier records. Stewart was the first to demonstrate in experimental rats that on hatching the young larvæ do not remain in the intestine but immediately bore through the wall and seek out first the liver and then the lung, traveling by the blood and lymph circulation and not through tissues. In the lung they desert the vessels and enter the air sacs. They migrate up the trachea and down the esophagus a second time into the stomach. This is the limit of their development in certain experimental animals like the rat, in which the worms are rejected in the feces. But in suitable hosts the young stages remain in the intestine and become fully mature.

Infection is evidently dependent on the chance ingestion of eggs in which the embryo is fully developed, for experiment indicates that before that time the eggs are not infective. Contaminated drinking water or food such as lettuce or radishes, imperfectly cleaned and eaten uncooked, may introduce the eggs into the human system. The eggs remain living and infective up to five years, at least, in water and probably longer in moist earth.

Distribution.—Long before Stewart's discovery in 1916 of the migration of Ascaris larvæ, Mosler in 1867 and Lutz in 1888 had observed the occurrence of pulmonary symptoms in man following the experimental ingestion of Ascaris eggs. Ransom and Foster demonstrated experimentally that the migration of large numbers of Ascaris larvæ through the lungs may produce pneumonia in pigs, being the cause of a malady known as "thumps," which is prevalent and highly destructive in young pigs.

While the mode of life and food habits render the human host less likely than the pig to acquire a heavy infection and hence a massive invasion of the lungs, it is evident that children are most closely in contact with the soil, and especially in rural regions most liable to infection from earth heavily polluted by swine. These conditions accord fully with the records of the occurrence of *Ascaris lumbricoides* in the human host. This worm is practically universally present among children in unhygienic, tropical and subtropical countries; among the nations giving most attention to hygienic conditions, it is a country parasite and is usually rare in the city population.

In the Medical Polyclinic at Bonn a marked increase in parasitism among city children was noted after the war. During the war *Ascaris lumbricoides* increased greatly in numbers in Switzerland also, according to Steiner. Scarcity of food and fuel and the use of human fertilizer in agriculture were probably responsible. Some children acquired very heavy infections and in these cases the school teachers noted a decided decline in mentality.

Experimental Infection.—In some experiments by Koino 500 eggs were administered to a robust man of 21 in whom on the ninth day a slight pneumonia developed. Koino also took 2000 eggs, which caused a slight fever on the third day, with chills on the sixth day lasting nine days, the maximum temperature being 104°F. (40.2°C.). Larvæ were recovered from the sputum on the third day, becoming more numerous until 178 were counted in 155 c.c. of bloody sputum on the fifth day. After that pneumonic symptoms were so severe as to endanger life. Ascaris pneumonia ordinarily lasts from three to eight days and its seriousness depends directly on the number of larvæ present.

While migrating through the tissues the larvæ molt. At the end of 50 days after the test feeding they have attained a length of 3 to 8 cm. and are still immature.

Ransom* has demonstrated how the Ascaris larvæ may reach various locations in the liver, spleen, lymph-nodes, thyroid, brain, and kidneys, as well as the lungs, by which the normal life cycle is fulfilled. Even small numbers in such places may have serious effect, despite the fact that they may not lead to the development of mature adults in the intestines. Fülleborn has obtained such larvæ in the brain of experimental animals. Sekiya found Ascaris larvæ in the urine of a child 11 months old who had been brought to the hospital with symptoms of typhlitis.

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* Ransom, B. H., Ascariasis. J.A.M.A., lxxix (Sept. 30, 1922), pp. 1094–1097.

Susceptibility of Hosts.—The young host is evidently more susceptible to Ascaris infection and hence more liable to suffer from pulmonary troubles consequent thereto. In the pig this has been studied intensively. It appears that as the animal grows older a certain immunity develops, generally in a few months or, to a degree, within a few weeks. When older pigs ingest ripe ova of Ascaris, the larvæ, which hatch in the intestine, seem unable to effect a migration and attain the adult stage. This resistance or immunity is apparently related to age and not to previous infections, but its basis has not yet been explained. Prophylaxis against ascaridiasis in pigs has been developed by utilizing this decrease in susceptibility to infection. A somewhat similar decreasing susceptibility with advancing age has been observed in the human host, but it is perhaps not so noticeable since infections are not so massive and may never become so fully established. In any event, it is not difficult to explain the differences in degree of infection between children and adults on the basis of habits and resulting exposure to infection.

Race incidence has not often been studied but G. C. Payne records data from 40,482 persons examined in Trinidad: East Indian 87 per cent. infected, Black 69 per cent., Creole 66 per cent., Yellow 62 per cent., Red 96 per cent., Unclassified 70 per cent., White 30.5 per cent. These ratios conform roughly to the regard for sanitation and the hygienic conditions prevalent among the races cited. These ratios are higher than those found among adult swine in the U. S. A. where records of the Bureau of Animal Industry show Ascaris to be present in about one-third of the hogs examined.

Pathology of Ascariasis.—One may group the pathologic effects of ascariasis under four subheadings: (1) Mechanical destruction of tissues during its wanderings; (2) introduction of infection as a consequence of these migrations; (3) production of bronchopneumonia by the larvæ, and (4) influence of dangerous toxins. While in the recent past the presence of these parasites has been regarded as a minor ailment, such an attitude is no longer possible in view of the rapidly accumulating evidence of their serious and even fatal influences, both direct and indirect, especially in children.

In experimental animals Yokogawa has demonstrated that the pathologic changes caused by the migration of Ascaris larvæ proper in the host do not differ from those due to foreign larvæ. While such changes have not been observed in the human host, in various experimental hosts there were produced marked and serious pathologic changes in the intestinal wall, in mesenteric and peripheral lymph-nodes, in the liver, lungs, kidney, brain and spinal cord; and these are apparent to the unaided eye in severe infections.

From its normal seat in the duodenum, the adult parasite often wanders into the stomach and may continue into the esophagus and pharynx. From this point, worms may enter the larynx with fatal results. Branch* says that these worms are commonly passed by nose or by mouth from young children. Migrating farther, the worms have been known to enter the Eustachian tube, to pass through the middle ear, piercing the tympanum and emerging from the external auditory meatus. Or the route chosen has involved the nasal passages and the tear duct so that the worm came out at the inner angle of the eye.

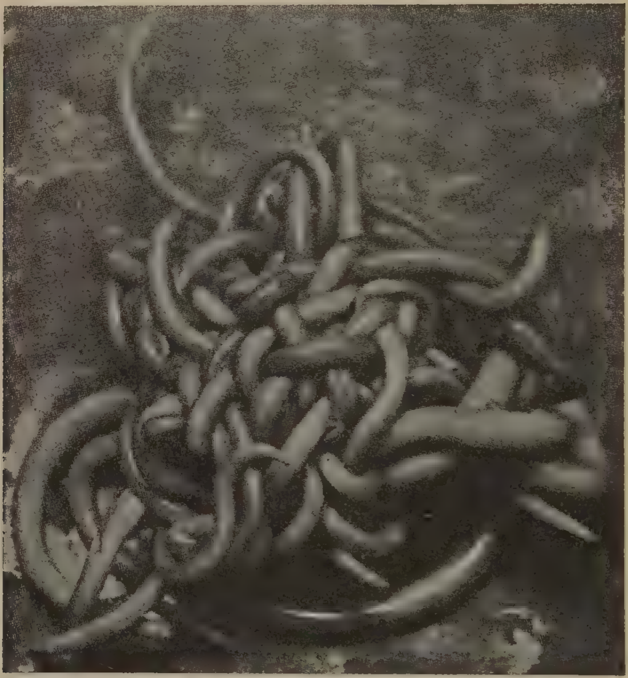

Fig. 387.—*Ascaris lumbricoides*. Mass of approximately forty worms, expelled in a case of acute intestinal obstruction. ×1.5. (After Perret and Simon.)

But the parasite does not always confine itself to normal passageways; it has been observed in abscesses well removed from the alimentary tract. Such an abscess may be intra-abdominal, as in a case reported from Holton, Maine, by Jackson.† Another is recorded in an infected infant only 22 months old. Also an ascarid was found in a pleural cavity abscess in a baby girl 2½ years old and in a boy of 11; and one in the scrotum of a boy of seven. The emergence of ascarides through the abdominal wall is recorded in many cases. In children the worms usually escape through the umbilicus, and in adults from the inguinal region, although the reverse may be true. In a few instances it is likely that a persistent omphalomesenteric duct served to aid the escape through the umbilicus.

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* Branch, C. W., Notes on Uncinaria and other Intestinal Parasites in the West Indies. Jour. Trop. Med., viii (Sept. 1, 1905), p. 261.

† Jackson, F. H., Intraperitoneal abscess containing roundworms. J.A.M.A., lxxii (Feb. 8, 1919), p. 412.

Both the normal and the abnormal routes described lead to conditions that may demand surgical interference. An impacted mass of ascarids has often been the cause of intestinal obstruction in children. This mass is frequently located a short distance above the ileocecal valve and may consist of from 16 to 60 entangled worms (Fig. 386). A typical case is described by Perret* in a white girl, aged eight years (Fig. 387).

Surgical Importance.—*Ascaris lumbricoides* is of some surgical importance in that it may cause ileus, spasm, invagination or perforation. While a knot of tangled worms is ordinarily responsible, fatal cases due to a few worms, or even to a single parasite, are recorded by various authors. In such a case, spastic contraction may lead to complete closure of the lumen. This spasm is thought to be due to mechanical excitation of the intestinal wall by the powerful movements of the parasite, to the damage done by the three toothed lips, or to secretions (excretions) that stimulate the muscularis chemically. Cases of enterospasmus verminosus are listed and discussed by Schaal.† They are more frequent among children, perhaps because the canal is narrower and more sensitive. McGlannon reported the case of a white girl of four with severe anemia, who was operated on for acute intestinal obstruction; two intussusceptions were discovered and in each was a roundworm.

The presence of the parasite in the appendix has been noted on various occasions. Hakansson‡ noted in such a case in a young girl that the appendix was in an advanced stage of inflammation: Many worms were in other parts of the gastro-intestinal canal. Many other similar cases are on record.

The entry of Ascaris into the bile duct may cause partial or complete obtruction. Most of such cases are among patients in later life, but a fatal case in a baby of two, and two relieved by operation in children of 12 and 7 , are reported. In 152 cases in the Philippines, the worms occurred five times in the liver and twice in the gall-bladder, but migration was probably stimulated by abnormal conditions of the bowel as all of these patients died of cholera. When the bile duct is invaded, the parasite may penetrate the tissues of the liver, in which specimens were found by Crowell and Hammack in two cases from the Philippine Islands. In another instance, ova, but no adult forms, were discovered in sections of the liver of a child of three years.

Operations on children are so seriously complicated by ascarids that treatment to eliminate them should be undertaken in advance. In a case of operation for intestinal sarcoma in a boy of eight, the ascarids later tore the suture open, invoking a fatal peritonitis. Apparently healthy children, operated on for hernia, dislocation, or adenoid growths, have suffered similarly. It appears that ordinary chloroform intoxication is aggravated by helminthiasis.[*]

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* Perret, J. M., Roundworms. J.A.M.A., lxviii (Jan. 27, 1917), p. 244.

† Schaal, Enterospasmus verminosus. Muenchener med. Wchnschr., lix (Nov. 26, 1912), p. 2619.

‡ Hakansson, E. G., Ascariasis and appendicitis; report of a case. U. S. Nav. M. Bull., xiv (July, 1920), p. 394.

Massive infections with Ascaris result not infrequently in death. This may be due to acute intestinal obstruction, perhaps complicated by perforation and gangrene of the bowel. Death from cerebral intoxication before the worms could be removed is also recorded. Surgeons have reported cases of suffocation by ascarides, and one death following administration of a vermifuge is ascribed to the blocking of the larynx by worms; 10 hours after death the worms were still issuing from the mouth.

Symptoms of Ascariasis.—A light infection with Ascaris may pass unnoticed, but if the parasite be present in larger numbers and for an extended period, its effects are manifested. The symptoms are not characteristic in most cases; they include fever and pain in the umbilical region, resembling early peritonitis or appendicitis with pronounced tenderness and other local symptoms. Cases are also pronounced "typhoid." In more extreme cases, emaciation, often pronounced, tympanic abdomen, general pain and depressed physical condition, are observable in the child. The blood usually shows an eosinophilia of 8 per cent. or even more, and the presence of the characteristic ova in the feces indicates the cause of the discomfort. The symptoms simulated those of peritoneal tuberculosis[†] in one case of extreme infection. Both abdominal and pulmonary symptoms disappeared promptly on removal of the worms. The presence of ascarids in a child may also give rise to symptoms resembling those of intussusception. Among other symptoms noted in some cases were urticaria and contusiform dermatitis. The lesions were obvious but disappeared promptly on removal of the worms.

Differential Diagnosis.—Confusion and even positive errors in diagnosis are likely, and attention should be called to the chance for mistake in the diagnosis of appendicitis, pneumonia, Ascaris, or hookworm. During certain stages these four conditions may easily be confused. Stiles cites an instance in which an excellent clinician made a diagnosis of pneumonia in four children of one family who later proved to have heavy infections with Ascaris. Hookworm infection, as well as Ascaris, can be diagnosed both as pneumonia and as appendicitis.

Toxic Effects of Ascaris.—These effects are often severe. Jos. Leidy II[‡] has recently published an account of toxic cases in boys of five and nine, and in a girl of 12. It cannot be doubted that *Ascaris lumbricoides* produces toxic symptoms in the host and on the hands of those dissecting the worms. In the search for the cause of toxic symptoms produced by these worm, various substances have been isolated and tested experimentally. Shimamura and Fujii isolated askaron, which they obtained in largest amount from coelomic fluid but also from other regions. It is regarded as a product of protein metabolism in the parasite. Experimentally its injection produced respiratory and renal disturbances, with fall of body temperature and blood pressure. However, it seems to be merely a metabolic product that happens to be toxic and its effects under conditions of parasitism are doubtful. Since this effect is certainly variable and possibly absent in some cases, the suggestion has been made that only on the death of the parasite is the toxic material set free.

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[*] Brun, V., Helminths complicating operations on children. Policlinico, xix (Oct. 6, 1912), p. 1481; Abstr. J.A.M.A., lix (Nov. 9, 1912), p. 1757.

[†] Pessoa, S. B., Severe ascaris infestation. J.A.M.A., lxxviii (April 29, 1922), p. 1294.

[‡] Leidy, Joseph, II, The hemotoxins of intestinal parasites. J. Parasitology, x (March, 1924), p. 149.

Flury who investigated intensively the toxicology of Ascarides (Arch. exp. Path. and Pharm., lxvii (1911), p. 275) found a series of metabolic processes characteristic of anoxybiotic life. Substances producing local irritation include volatile aldehydes, of the oleic acids, free volatile oleic acids themselves, and acid esters of the ethyl, butyl and amyl series. The continued formation of such substances may cause injury and destruction of the intestinal mucosa. Chronic acid poisoning in Ascaris carriers and affections of the central nervous system may be expected as the result of the constant resorption of volatile substances of the oleic series. All the affections of this type described, *viz.* chorea, hysteria, epilepsy, tetanus, cramps, mental disturbances, may easily be explained by the chronic intoxication of aldehydes alone and especially toxic is valerianic acid which is produced in large amounts.

Cases of severe intestinal infection with Ascaris in children are accompanied at times by acute nervous troubles which are presumably due to toxic substances.

The susceptibility of non-carriers to the external influence of Ascaris is marked. Ransom* finds that an aqueous extract of *A. lumbricoides* commonly provokes eye symptoms (irritation, lacrimation, and swelling of the eyelids) and an urticarial skin reaction. There may be a severe general reaction if the extract reaches any abrasion of the skin. Some nonreactors gave a definite history of Ascaris infection. When living worms are handled in the laboratory, the toxic effects of the Ascaris fluids are so severe in the case of susceptible persons that the absorption of minute quantities gives rise to alarming symptoms, and also disturbs the equilibrium of the blood, as shown by changes in the number of leukocytes.

Treatment.—Santonin is a favorite remedy against roundworms. According to Stevens, "it does not kill the parasites, but through some inimical influence causes them to migrate to the colon, whence they may be expelled by a cathartic. The drug may be prescribed in lozenges or in powders, mixed with a few grains of sugar." The diagnosis having been confirmed, a good plan is to cleanse the bowel at night, giving the santonin the next morning and evening, followed the day after that by a brisk cathartic; best in this relation is calomel. De Buys* suggests the following doses of santonion for various ages:

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* Ransom, B. H., Harrison, W. T., and Couch, J. F., Ascaris Sensitization. Jour. Agr. Res., xxviii (May 10, 1924), pp. 579–584.

Six months 1/12–1/6 gr.	0.005–0.01 gm.
One year 1/6–1/3 gr.	0.01 –0.02 gm.
Eighteen months 1/4–1/2 gr.	0.016–0.03 gm.
Two years 1/3–3/4 gr.	0.029–0.048 gm.
Three years 1/2–1 gr.	0.03 –0.065 gm.

The following prescription modified according to the age of the patient may be employed.†

	Gm.	C.c.	
Santonini	0	30	gr. v
Hydrargyri chloridi mitis	0	20 or	gr. iii
Sacchari lactis	3		gr. xiv

M. et fac. Chartulas 10.

Sig.: A powder, in water, every hour for 3 doses.

Oil of chenopodium is considerably more effective than santonin for roundworms. The dose for a child aged five years is two drops on a lump of sugar, accompanied by a generous dose of castor oil, repeated at two-hour intervals, if necessary. The drug is distinctly constipating and toxic. Its most active anthelmintic constituent is ascaridol of which 1 c.c. is adequate to remove ascarides from an adult.

Other Species of Ascaris Occasional in Man.—*Ascaris maritima* was found once in the vomit of a child in North Greenland in 1865. It was probably ingested with the viscera of some food animal and should be ranked as an erratic parasite.

At one time investigators were inclined to recognize as a separate species *Ascaris suum* sive *suilla* from the pig. But frequent careful comparisons have failed to disclose any morphologic differences. Complement fixation tests by Bakker (Tijd. v. vergl. Geneesk., 6:160, May 30, 1921) show that Ascaris from man and that from the pig act reciprocally in identical fashion. *Ascaris ovis* from the sheep is apparently an erratic form of *Ascaris lumbricoides* which can maintain itself in that unusual host. But it does not thrive, as no female has ever been found which contained fertile eggs.

Belascaris cati (Schrank 1788) is a very common parasite of the cat which has been found nine or ten times in the human host.

Toxocara canis (Werner 1782) occurs abundantly in the dog, and was long confused with the foregoing species. It was found once in the human host in Egypt by Leiper.

FAMILY OXYURIDÆ Cobbold 1864

Meromyaria relatively small, transparent forms with simple inconspicuous lips. Female with much elongated caudal end; vulva anterior; eggs characteristically flattened on one side. Male with one spicule, which may be reduced, imperfectly chitinized, or absent.

The type genus Oxyuris is so large that some authors split it up into several; in this case the group containing the human parasite is known as Enterobius Leach 1853 (synonym: Oxyurias Stiles and Hassall, 1905).

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*System of Pediatrics, Abt. Vol. II, Page 334.

†Osborne, O. T. and Fishbein, Morris—Handbook of Therapy, Chicago A. M. A. 1923, p. 297.

GENUS OXYURIS Rudolphi, 1803

Two enlargements on esophagus. Male with single spicule and two pairs of pre-anal papillæ. Female with long pointed tail. Vulva in anterior part of body. Egg asymmetrical, smooth, thin-walled, and with well developed embryo when laid. Among many species parasitic in higher vertebrates, one occurs in man.

Oxyuris vermicularis (Linnaeus 1758)

Synonyms.—*Ascaris vermicularis* Linnaeus 1758; *Fusaria vermicularis* Zeder 1803; *Enterobius vermicularis* Leach 1853; *Fusarella vermicularis* Seurat 1916.

The cuticula of this worm is striated and forms dorsal and ventral projecting alæ near the head, also crests along the lateral lines of the body (Fig. 388). The esophagus is long, terminated by a distinct bulb with teeth. The male is from 3 to 5 mm. long, with a spirally rolled tail; there are six pairs of papillæ. The female is from 9 to 12 mm. long and 1 mm. broad, and the vulva lies just in front of the limit of the anterior fourth of the body. The eggs are elliptical and asymmetrical, measuring 50 to 56 by 30 to 32μ (Fig. 346).

Distribution.—The species has been known from remote antiquity as a cosmopolitan parasite of man, especially in early life. It occurs equally in all climates, but is more abundant in the city than in the country, and is most abundant in infants and children probably by virtue of the ease with which auto-infection takes place.

The adult pinworm inhabits the large intestine of man only, though Leidy's *O. compar* from the cat is possibly identical with *O. vermicularis.* The young worms live in the small intestine. Very young males and females have often been found in the vermiform appendix.

Life History.—This species does not usually oviposit in the intestine. When the uterus of the female is loaded with ripe eggs, the worm migrates into the rectum and may be eliminated with the feces, in which case the uterus is promptly evacuated. The egg mass, containing several thousand ova all in the same stage of development, is held together by the adhesive external layer of the shell. There is a second, thinner internal membrane, and within this lies a coiled embryo. The egg does not hatch until it is introduced through the mouth, when duodenal digestion brings about the release of the embryo and the beginning of growth. After two molts the worms pair, migrate into the large intestine, and complete the life cycle.

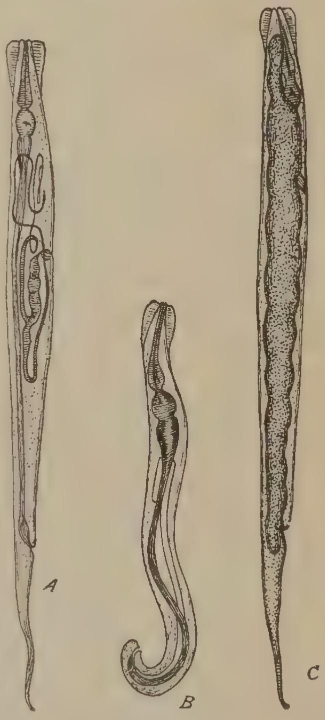

Fig. 388.—*Oxyuris vermicularis; a*, sexually mature female; and *b*, male; *c*, gravid female. Magnified. (After E. W. Koch.)

As the gravid females approach the anus they arouse an insufferable pruritus. They may wander out on the perineum and provoke scratching by the host. In this way eggs deposited by the females, or set free by their laceration during the scratching, contaminate the hands and are transferred to food, or in other ways by chance are carried into the mouth, achieving thus auto-infection of the host.

Mode of Infection.—Primary infection is brought about by the use of contaminated food eaten uncooked, *i.e.*, fruits or more probably vegetables, rather than by impure drinking water, as the eggs survive only a brief time in water. Perhaps flies are instrumental in distributing the eggs to new hosts by contaminating exposed food. The absence of a boring spine on the head of the embryo indicates that probably the larvæ do not carry out migrations through the tissues of the host but settle down at once in the intestine. The direct development is very rapid, as Leuckart experimentally obtained young worms from 6 to 7 mm. long fourteen days after ingestion of the eggs, and his observation has been confirmed by several later investigators.

Frequency.—While the seat worm has been noted in hosts of all ages from a few weeks to advanced years, it is much more frequent in children. Heller in Germany recorded its presence in 188 out of 1000 men, in 211 among 1000 women, and in 338 among 1000 children. Müller in Denmark listed it in 51 per cent. of men, 43 per cent. of women and 62 per cent. of children (less than 15 years) examined, the percentages obviously decreasing with advancing age. Recent statistics demonstrate that this parasite is much more common than formerly supposed, being found in 70 to 85 per cent. of rural school children in continental Europe. No acceptable statistics exist for the U. S.

Pruritus Ani.—Other Symptoms.—The most constant symptom associated with the presence of this parasite is pruritus ani of a periodic type, being marked in the evening on retiring as the parasites are aroused to activity by the warmth of the bed. This is associated with congestion of the anal margin and of the rectal mucosa. Migration onto the perineum accentuates the symptoms. In cases among young girls the worms have wandered into the vagina, producing enuresis, onanism and even incipient nymphomania. Even in the rectum the worms have produced reflex nervous activities and in some instances epileptic attacks. In certain cases, peculiar manifestations such as trichotillomania have been noted. The worms are responsible at times for nodules in the rectal wall, containing the ova of the parasite. Their presence in tuberculous nodules and tumors in surrounding tissues has also been demonstrated; this involved in one case a migration of 2 cm. or more through solid tissues.

Relation of Oxyuris to Appendicitis.—There has been much discussion on the possible causative rôle of Oxyuris in cases of appendicitis among children. In series of examinations made by various authors, this parasite was found in from 50 to 75 per cent. of all appendices extirpated from children less than 15 years of age. In one series

Rheindorf observed Oxyuris in the appendix at 6 out of 13 necropsies of children between 3 and 12 years of age who died from acute appendicitis. One can exclude a direct relation of Oxyuris to the primary infection, but must acknowledge a clear secondary relation. Evidently, however, it is important to keep the intestines of children free from this parasite.

Treatment of Oxyuriasis.—While in the past the treatment for pinworms has not been very satisfactory, recent years have seen some splendid advances. Previously one had to rely on astringent enemata for the removal of the female worms, which find their way to the lower part of the bowel, but the males and young were not affected and reinfection would continue to take place. Some of the well-known anthelmintics have been used with varying results, but when such substances as thymol, carbon tetrachloride and oil of chenopodium are used they have to be given over long periods of time or in repeated courses. Nyberg (Finska Läkaresöllskopets Handlinger, 1923, 65:354) cites more than eleven cases which he treated by having them eat 0.5 liter of fresh blueberries three or four times a day for the first day and for the next six make one meal a day of them. In all that he was able to hear from, the diet had brought about a cure. H. Hajos (Med. Klin. Berlin 1922, 18:1619) reported successfully treating seven adults by feeding them each 0.9 mg. of neo-arsphenamin. Perhaps the most successful treatment yet devised, one which has been confirmed by many workers, is to administer bismuth-carbonate by mouth in 10 gm. doses to adults on two successive days, 4 gm. doses to children of seven or 3 grm. doses to children of two years. The course may be repeated. This treatment was accidentally discovered by Leiper (Prog. Med. 1920, 35:339) while treating patients with duodenal ulcer.

The treatment appears to call, not for a single drug by mouth, but for a special diet, oral and rectal medical treatment, and salves, personal hygiene, etc. Aluminum salts, such as aluminum subacetate, appear to be valuable by mouth (Hall).

With any form of treatment, the hands of the child should be kept away from the anus. The bed clothes should be boiled every day, the night-clothes and underwear should be worn but one day and boiled before replacing; the night-clothes should be provided with tie-strings for the hands, and the child should be given a sponge or shower bath instead of a tub-bath (see Hutchinson). One per cent. thymol ointment will be found useful to apply locally to stop the itching.

Oxyuris incognita, which was named from the eggs discovered in the feces is not a true parasite. See *Heterodera radicicola* (p. 1016).

Syphacia obvelata, a related species of Oxyuris and a mouse parasite, has been reported by Riley from an American child living in the Philippine Islands. All five members of the family were heavily infected. This parasite may have been overlooked heretofore or confused with Oxyuris, as the chances for its introduction into the human host are evidently large under unsanitary conditions.

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